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Parallelism of Coccidioidal and Tuberculous Infections[1]

CHARLES EDWARD SMITH, M.D.

San Francisco, Calif.

PRIOR TO THE discovery of the etiology of "San Joaquin fever" (1) the comparison of coccidioidal infection and tuberculosis was restricted to the clinical and pathological mimicry of coccidioidal granuloma and tuberculosis of the reinfection type. The outstanding difference lay in the fact that there was but one recognized manifestation of coccidioidal infection, coccidioidal granuloma, which was, and still is, highly fatal. In contrast, reinfection type tuberculosis constitutes only a fraction of tuberculous infections. We now realize that this divergence was only apparent; it has given place to the most striking parallelism, since in both diseases mild and even subclinical infections are the rule and serious disease is the exception. It is the current status of this comparison that will be reviewed here.

In presenting this comparison, the etiologic agents constitute a logical starting point. In the rest of this paper I must be on the defensive and point out how my protégé resembles tuberculosis, but here, with great satisfaction, I can reverse the rôles. For the tubercle bacillus *is* fungus-like, else why the *Myco* of *Mycobacterium*? There is no suggestion that this relationship is close. The tubercle bacillus may have been accused of having a filtrable stage, but never has it masqueraded as an animal parasite. It never undergoes a spectacular metamorphosis such as *Coccidioides immitis* displays when its chlamydospores enter living animal tissue. The studies of Lack (2) and Baker and Mrak (3) suggest that spherule formation, the so-called "parasitic phase," is the response of *Coccidioides* to a less favorable environment. The tubercle bacillus, with much more consistency, just wraps its waxy coat around it and hangs on.

There are, nevertheless, additional points to consider. While mammals, birds, and reptiles have their own tubercle bacilli, and mammalian tubercle bacilli may be subdivided into bovine and human types, we have no evidence of such a situation with *Coccidioides*. *Coccidioides immitis* and the human type of *M. tuberculosis* are alike in that no evidence exists associating differences in severity of the clinical infection in man with strain differences of the organisms. Various investigators have remarked on apparent differences in strain virulence in laboratory animals, but admitted that no correlation exists with clinical pictures of the human illnesses from which the strains were isolated. We have never been able to demonstrate by animal inoculations, by cultural character-

[1] From the Department of Public Health and Preventive Medicine, Stanford University School of Medicine. The study has been supported by the Rosenberg Foundation of California.

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istics, or even by making and testing with specific coccidioidins, that the fungus of a coccidioidal granuloma patient differed from that of a patient with the erythema nodosum of "San Joaquin fever," or from that of another patient with transient respiratory symptoms. In this connection, the question has been raised whether the products of the fungus responsible for the coccidioidin reaction differ so that a false negative test might ensue. It is to be recalled that persons with coccidioidal granuloma frequently react poorly to coccidioidin in distinction to erythema nodosum "San Joaquin fever" patients, who react violently. In testing autogenous coccidioidins, we found on a number of occasions that a patient with granuloma reacted no more strongly to coccidioidin of *Coccidioides* isolated from an erythema nodosum patient than to his own brand, nor did the erythema nodosum patient react more strongly to his autogenous coccidioidin than to that of the granuloma patient. Kessel (4) came to the same conclusion in his studies on guinea-pigs. Our observations have been on man. Thus the relationship of the tubercle bacillus to tuberculin and *Coccidioides* to coccidioidin seems parallel.

PATHOGENESIS

The usual portal of entry for both tuberculosis and coccidioidomycosis is the respiratory tract. Occasionally, either of the infections may be acquired through the abraded skin. While tuberculosis may be acquired by ingestion, such is not the case with coccidiosis, although Ahlfeldt (5) reported some unconvincing results obtained by feeding rabbits lettuce doused with *Coccidioides*. In contrast to what is seen in severe pulmonary tuberculosis, coccidioidal granuloma enteritis is unknown even among patients putting forth consistently positive sputa. Stomach washings containing spherules of *Coccidioides* are usually negative after a few hours. Evidently the fungus does not withstand the rigors of the gastro-intestinal tract. The usual portal of entry, however, and the site of the subsequent primary focus are similar in the two infections.

Pneumonitis results in the respiratory symptoms which are frequently observed in primary coccidioidal infection. As in primary tuberculosis, roentgenograms frequently, but not always, show the lesion, and the fungus or bacillus may be found in the sputum or stomach washings. Then follows sensitization to the filtrable products of the responsible organism. The time required to develop sensitivity to coccidioidin seems to be approximately the same as for tuberculin. Wallgren (6) gave an average figure of four and one-half weeks from exposure to sensitivity to tuberculin, with a range from three to eight weeks. We know (7) that the incubation period for primary coccidioidomycosis is one to four weeks, averaging from ten days to two weeks, while an average of one to two weeks longer (from two days to four weeks) is required for development of sensitivity. In the usual primary infection the primary focus is walled off by the host without complication and the only evidence is a resultant positive skin test and sometimes a calcified pulmonary nodule. It must be admitted that for primary coccidioidomycosis these stages have not been demonstrated anatomically, but clinical and roentgenologic evidence clearly indicate that sequence. Moreover, we (8) have demonstrated arrested pulmonary lesions of coccidiosis, some of them calcified, which both by roentgenography and at autopsy were mistaken for tuberculosis. Recently we recovered viable *Coccidioides* from one such lesion.

Occasionally in both infections erythema nodosum develops. When it appears in coccidioidal infection, the syndrome is known as "San Joaquin fever." The evidence which we have assembled (7) is in complete accord with the theory championed especially by the Scandinavians. This may be summarized as follows: When allergy is first established, sensitivity is at its peak and may be manifested or at least associated with erythema nodosum. The skin lesion constitutes a non-specific aller-

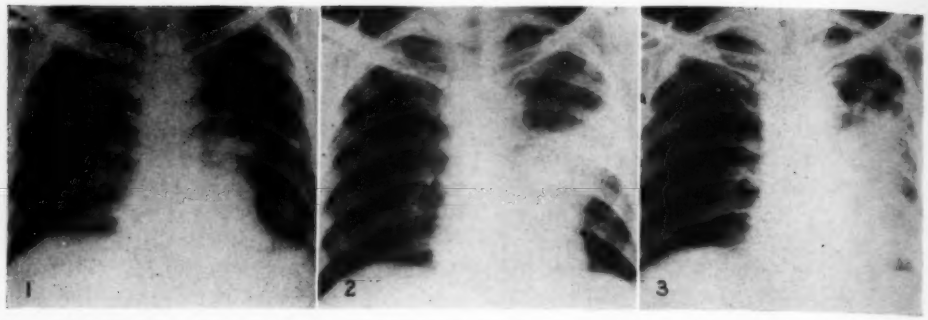
gic manifestation of a specific sensitization. Time relationships show conclusively that coccidioidin sensitivity is established just prior to the erythema nodosum. Frequently production of a crop of erythema nodosum lesions by an injection of tuberculin has been observed. Wallgren (6) attributed this to an undulation of the allergic level such as is observed when the allergy is first established. Kessel (9) produced a recurrence of erythema nodosum in a patient convalescent from "San Joaquin fever" by giving him the dose of coccidioidin which he was accustomed to administer to his granuloma patients. We had a comparable experience. A young man who suffered an attack of acute coccidioidomycosis without erythema nodosum came to us from Coalinga three weeks after onset. His convalescence continued without complication for another three weeks. He chanced to come into the laboratory one day while we were checking on ourselves the potency of two lots of coccidioidins which had experienced the exigencies of two years of San Joaquin Valley car temperature. Being co-operative, he volunteered his services, too. We each received three different 0.1-mg. doses and one 1.0-mg. dose of coccidioidin. That night he had a considerable systemic reaction and for the next three days blossomed with erythema nodosum. Perhaps these eruptions come as a result of undulating allergy, but there is some suggestion that the lesions are actually the result of circulating antigen in a hypersensitive person. Time after time a "valley fever" patient remarks that the coccidioidin reaction feels, as it looks, like one of "the bumps," and frequently the reaction in a patient with erythema multiforme shows satellite vesicles like erythema multiforme.

Apparently the frequency of erythema nodosum in primary coccidioidomycosis is greater than in primary tuberculosis. However, it rarely recurs. Only two of 432 cases of "San Joaquin fever" may have been second attacks (7), and even they were doubtful. This apparent immunity is understandable when one realizes that the allergy is of long duration. Residents of the San Joaquin Valley tested as long as twenty-one years after an attack of "valley fever" have exhibited very strong coccidioidin reactions. The objection may be raised that in these persons the allergy was maintained by repeated exposures. However, our first laboratory victim, Dr. H. D. Chope, though he had been out of the laboratory and was therefore no longer subject to occupational exposure, reacted violently to 0.1 mg. coccidioidin nine years after his infection was acquired. The probable explanation of this continued sensitivity is the arrested lesion mentioned previously, common to both infections. Thus the *sine qua non* of erythema nodosum, a change from negative to positive reaction, cannot take place.

When we come to a comparison of the pathogenesis of coccidioidal granuloma and tuberculosis of reinfection type the problem becomes somewhat difficult. It does seem quite certain that coccidioidal granuloma is due to reinfection. Our coterie holds that the mechanism is *endogenous*, a dissemination from the primary focus at the time of the initial infection (usually) or later (less frequently). This consideration is of practical importance, for were we even suspicious that exogenous reinfection resulted in coccidioidal granuloma, we should have to order every person out of the San Joaquin Valley as soon as he had his primary infection. Ere long it would revert to jackrabbits and ground squirrels. However, far from believing that an initial infection predisposes to granuloma, we feel that it confers a lasting immunity, at least to exogenous infection. The reasons follow:

(1) Infection with *Coccidioides* is acquired rapidly in the San Joaquin Valley (7). This fact indicates that exposures are frequent. If re-exposures cause granuloma, most of the inhabitants of the Valley would have granuloma.

(2) We have had 21 laboratory infections, 12 indicated by positive coccidioidin reactions when the test was first performed. Nine others who joined our ranks subse-



Figs. 1–3. Coccidioidomycosis, Case of I. B. 1. Chest roentgenogram five days after onset of symptoms of primary coccidioidomycosis. 2. Chest roentgenogram eight days later (thirteen days after onset), showing increase in size of lesion. 3. Chest roentgenogram nine days later (twenty-two days after onset) with further increase in size of lesion, development of pleural fluid, and evidence of hematogenous spread to right lung.

quently have rapidly been infected, as indicated in 5 cases by a shift from a negative to positive skin test and in 4 others by actual recovery of the fungus. A new worker gets his infection in from two to four months. Repeated exposures must occur. Not only have none of us developed granuloma, but our serology remains negative and none of us have had any symptoms remotely suggesting those of a second "primary" infection.

(3) Laboratory animals, after one infection, are resistant to reinfection.

(4) The nearest approach to human reinoculation occurred when 14 Stanford naturalists took a field trip to San Benito County a year and a half ago and 7 developed primary coccidioidomycosis. This first recognized epidemic of coccidioidal infection has been reported by Doctor Davis and his colleagues (10). The roentgenographic aspects of the outbreak were carefully followed by Doctors Starks and Powers (11), who have reported them independently. When we checked the activities of the 7 victims, we found that the only place where all were congregated was in digging out a rattlesnake in the Panoche Valley. Incidentally, *Coccidioides* was recovered from the soil of this rattlesnake nest. Two others of the group who were in the midst of the digging escaped. When the group was rounded up, both of the "escapes" had positive coccidioidin tests, but their normal sedimentation rates, blood counts, precipitin and complement fixation tests ruled out the possibility of currently active infection. One was an habitual "field tripper" with many sorties to the San Benito district and the San Joaquin Valley to her credit. The other had taught at McFarland, Kern County, nineteen years before. While there, he experienced an illness which a Bakersfield physician diagnosed as tuberculosis. He was sent to a sanitarium for several months, but tubercle bacilli were never found. Doubtless both of these persons had already undergone primary infection.

(5) While coccidioidal granuloma may affect any organ (except the epithelium of the intestinal tract) in a manner clinically and pathologically indistinguishable from tuberculosis, the most frequently encountered lesions are those characteristic of a hematogenous spread.

Thus there is considerable evidence that exogenous reinfection with *Coccidioides* is not important. On the other hand, one frequently obtains an account from a granuloma patient of what sounds like a typical initial infection, but the patient, never recovering, goes directly into coccidioidal granuloma.

Two examples of this progression of primary infection to coccidioidal granuloma follow. Both patients were male Filipinos.

I. B.[2] was a patient of the Tulare Gen-

[2] Appreciation is expressed to the staff of the Tulare General Hospital for their co-operation in providing these data.

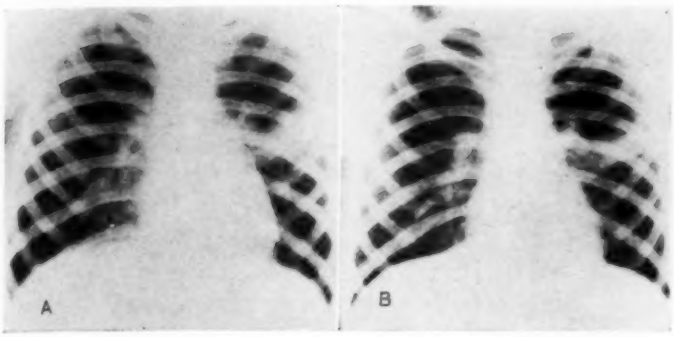


Fig. 4. Chest roentgenograms showing pulmonary density due to primary coccidioidomycosis. A. Roentgenogram made twenty-three days after onset of symptoms. B. Three weeks later; definite regression in size of shadow.

eral Hospital. In September 1940, three years after going to the San Joaquin Valley, he came to the hospital acutely ill. The onset with chill and fever, cough, and pain in the left chest made worse by breathing, and the admission diagnosis of "pleurisy" were characteristic of primary coccidioidomycosis. The recovery of *Coccidioides* from the sputum established the diagnosis. The roentgenogram taken just five days after the onset of symptoms is typical of the initial infection (Fig. 1). Eight days later, however, the process had extended and smaller foci had appeared in the upper lobe (Fig. 2). Nine days later, only seventeen days after the original film and three weeks after the onset, the infiltration had involved most of the left lung and fluid had formed (Fig. 3). The patient subsequently signed himself out of the hospital but returned to die less than three and one-half months after onset. The clinical history and roentgenographic evidence both mark this patient as having failed to focalize his infection. In contrast are roentgenograms of two patients with primary coccidioidal infection in whom the infection was arrested (Figs. 4 and 5).

Since the first patient had lived in the endemic area three years, the objection may be raised that he may have already had his initial infection and that this three-month illness was an exogenous reinfection.

The second Filipino, never in the San Joaquin Valley until August 1938, then went to pick grapes near Arvin. He lasted nearly a month, but the heat drove him back to Monterey County. About two weeks after his return, cough, malaise, fever, and night-sweats developed. He went steadily downhill. In January 1939 he had right lower quadrant pain, for which an appendectomy was performed. An ulcer was found on the mesoappendix and the peritoneal surfaces were studded with tubercles, apparently due to tuberculous peritonitis. However, the vigilant pathologists proved that it was not tuberculous but coccidioidal peritonitis. This patient could not possibly have had an exogenous reinfection responsible for his coccidioidal granuloma.

Thus, as in tuberculosis, the ability to localize a coccidioidal infection seems to depend on some unknown quality of the host, including such factors as sex and race.

SUMMARY

To summarize, *Mycobacterium tuberculosis* and *Coccidioides immitis* have several points in common. There is no correlation between the severity of the clinical pictures in the human cases from which strains are isolated and pathogenicity. Moreover, tuberculin and coccidioidin for the respective skin tests, while specific for each, do not exhibit "strain" differences.

The principal portal of entry of the two infections is alike, the respiratory tract. The subsequent localization, pneumonitis,

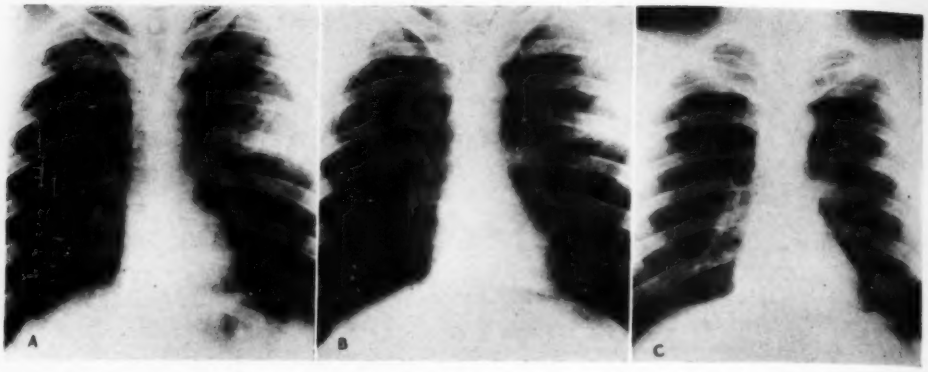


Fig. 5. Chest roentgenograms showing regression in size of pulmonary density due to primary coccidioidal infection. A. Roentgenogram taken two months after onset. B. Three months later (five months after onset). C. A year and a half later: practically complete resolution. Only a fibrous band remains at the site of the consolidation.

development of allergy, and focalization of the primary infection are also similar. In both the result may be a walled-off lesión, which may calcify.

The erythema nodosum of primary coccidioidomycosis, like that associated with primary tuberculosis, occurs very soon after allergy is first established, when the patient is hypersensitive. It may possibly be a reaction of these very sensitive tissues to circulating antigen. Post-primary erythema nodosum due to either infection is rare.

The pathogenesis of coccidioidal granuloma seems to be that of an endogenous reinfection. Evidence is presented that the primary infection of *Coccidioides immitis* not only does not predispose to the granuloma but actually confers a lasting immunity to exogenous infection. As in tuberculosis, the ability to focalize a coccidioidal infection seems to depend on some unknown quality of the host.

2330 Clay St.
San Francisco, Calif.

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The Roentgen Diagnosis of Fungous Infections of the Lungs with Special Reference to Coccidioidomycosis[1]

RAY A. CARTER, M.D.
Los Angeles, Calif.

THE PURPOSE of the present paper is to reconsider the roentgen manifestations of coccidioidal infection of the lungs, and to attempt comparisons with diseases, mycotic and otherwise, which may simulate it.

Conceptions of the disease have been revolutionized by the proof, by Dickson, that primary pulmonary coccidioidomycosis is a spontaneously recovering disease, widespread in the San Joaquin Valley of California, and by further studies of its behavior, clinical, pathological, and epidemiological. Cases have accumulated since our previous reports (2–4) confirming some impressions, modifying and correcting others.

The clinical, mycologic, pathologic, allergic, and epidemiologic aspects of the disease will be discussed only as they appear necessary to a roentgenologic presentation. These topics are covered elsewhere in this symposium and in the literature.

Some recent studies of importance may be mentioned. Primary coccidioidomycosis has been described by Dickson and associates (6, 7, 8, 9, 11); its epidemiological features, by Smith (22); sensitivity tests, by Kessel (17), Stewart and Kimura (23), and Thorner (24); therapy, particularly immunotherapy, by Jacobson (16).

Many cases are required to type a disease, roentgenologically as well as otherwise. Even then unusual and confusing manifestations arise. Although primary coccidioidomycosis is widespread in its restricted location, cases studied roentgenographically are relatively few. In the comparatively infrequent secondary form, the number of cases is still inadequate. Our own series of this stage, probably larger than can be assembled in any one institution, may establish clear predilections, and illustrate most manifestations likely to be encountered. It is inadequate for close differentiation, and particularly to establish roentgenologic grounds for proof or elimination of the disease. The positive diagnosis still rests mainly upon the identification of *Coccidioides immitis*.

PRIMARY COCCIDIOIDOMYCOSIS

It has been known for many years that the initial infection is far most commonly pulmonary, and that this need not lead to the generalized disease. In 1930 we saw the films of two such cases, through the courtesy of Dr. Philip Pierson. Prior to the identification of valley fever, the tendency was to attribute the few recoveries which were observed to early recognition and treatment. Chamberlain, however, in discussion in 1930, said: "I suspect that cases occur with rapid recovery, without identification of the organism" (2).

A clear history of the frank influenza- or pneumonia-like primary attack and roentgenograms are available for only a small proportion of those reacting positively to the coccidioidin vaccine. Roentgenographic series will be heavily weighted with patients whose respiratory attacks have been clinically severe, or who have had an erythema nodosum. As in tuberculosis, the immediate allergic response to the primary infection (including the erythema nodosum) does not necessarily parallel the severity of the attack. The roentgen manifestations, however, presumably do.

Death appears to occur rarely, if ever, from the primary invasion, except by direct progression into a secondary metastatic stage. We are therefore indebted to Cronkite and Lack (5) for a conception of

[1] From the Department of Radiology, Los Angeles County Hospital, presented as part of a Symposium on Fungous Infections before the Radiological Society of North America, at the Twenty-seventh Annual Meeting, San Francisco, Calif., Dec. 1–5, 1941.

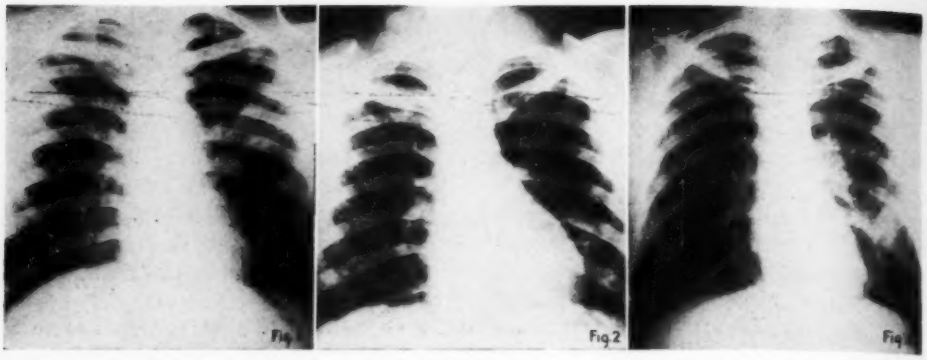

Fig. 1. Primary coccidioidomycosis with cloudy infiltration and with lymph node enlargement in its drainage path. The parenchymal and node involvement resolved partially in the following month.

Fig. 2. Primary coccidioidomycosis with a cavity surrounded by "mottled" infiltration. The cavity disappeared within six weeks. Slight node enlargement, however, became evident while the parenchymal involvement regressed.

Fig. 3. Residual discrete nodal density and slight lymph node enlargement several months after recovery from primary coccidioidomycosis.

the primary pulmonary pathology. By inhalation infection of the guinea-pig, they found the lesions to be of tubercular structure, quite tuberculosis-like micro scopically. These involved the lungs and tracheobronchial lymph nodes, and became associated with fibrosis and necrosis. In the human disease, therefore, we may anticipate an associated adenopathy, and slow or incomplete regression of parenchymal lesions.

Detailed roentgen characterization of the primary coccidioidomycosis must await repeated observation of many cases, over periods far past the time of clinical illness. This will come from the San Joaquin Valley.

A few patients with primary infection have entered our hospital since the spontaneously recovering disease has been known. A few others may be identified in retrospect. We have been privileged to study other cases through the courtesy of Dr. Johnson of the Kern County General Hospital, and of Drs. Hoffman, Butt, Smart, and Taylor of Los Angeles. Powers and Starks have reported on 7 cases from the roentgen point of view (21). Roentgen descriptions are available in other articles written primarily from a clinical standpoint (6, 7, 8, 9, 12, 13). It has been emphasized by several that films are not usually available early in the attack. Provisionally, the following statements may be made.

Parenchymal involvement of several types may be seen in any part of either lung. Areas of "peribronchial thickening" or "fuzzy shadows" radiate from the hila, usually, but not necessarily, toward the bases. There may be zones of diffuse unorganized cloudy density; scattered hazy foci of infiltration of a type often described as "mottling" (Fig. 1); hazy or discrete nodal densities; or infiltrations, confluent to the degree of partial or complete consolidation. These consolidations are not usually fully lobar in extent or distribution. Lesions may be solitary or multiple, and different roentgenographic types may be seen in the same chest. One or more cyst-like cavities may appear in zones of infiltration (Fig. 2).

Lymph node enlargement—mediastinal, hilar, or both—is evident in a typical case, occurring or accentuated in the drainage path of visible parenchymal lesions (Fig. 1). Pulmonary lesions limited to the "peribronchial" type appear less likely to be associated with visible adenopathy. As may occur in primary tuberculosis, the adenopathy may become evident after the pulmonary lesions are seen and may increase while the latter are regressing.

Advanced adenopathy is not readily missed. Slight enlargements require the recognition of small "lumpy" deformities of the hila and aortic contours. Widmann (26), in discussing tuberculous adenopathy, cites the importance of its early recognition.

Pleural involvement may accompany the parenchymal lesions. It is usually local, interlobar or parietal, plastic in appearance, and adjacent to evident parenchymal foci. It may occur early, since the onset of the attack is frequently associated with thoracic pain (8).

The parenchymal and lymph node lesions tend to regress slowly over a period of weeks or months. Lesions which are wholly "peribronchial" may regress quite rapidly and completely, together with any associated adenopathy. Cloudy foci or consolidations, complete or partial, appear to regress more slowly, and may leave residual linear or heavy strand shadows of fibrotic appearance, or discrete areas of density, at times with pleural thickening. These may remain indefinitely, with or without the persistence of lymph node enlargement (Figs. 3 and 9). The majority of involvements clear up completely.

Cavities may disappear within a few weeks or may persist indefinitely. In the latter case, the initial adjacent infiltration may subside, leaving fibrotic-appearing strand-like shadows, as in tuberculous cavities, or may disappear completely, leaving an isolated thin-walled cavity resembling a congenital cyst. In one of our cases (Fig. 2) a cavity disappeared sufficiently rapidly to suggest that local air trapping and formation of a pneumatocele may sometimes be the mechanism responsible, as described by Peirce (20). Under this conception, the persistence of the cavity may be considered to depend upon the degree of infection of the pneumatocele. In one case the organism was recovered from a residual "cyst" after lobectomy. No other sign of infection was present at the time of operation, although coccidioidal empyema developed. The patient made an apparently complete recovery.

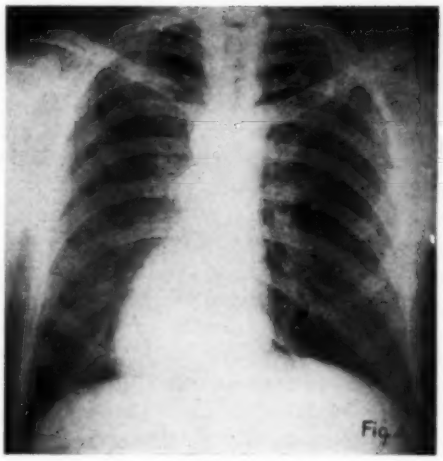

Fig. 4. Apical linear strand shadows and thin-walled cavities, without lymph node enlargement. Such lesions may be residual from primary coccidioidomycosis or tuberculous.

Lymph node and parenchymal calcifications containing *Coccidioides immitis* have been found at autopsy in patients having no evidence of the secondary disease. These must be assumed to have resulted from the primary infection (Butt, personal communication). Richard Taylor (personal communication), seeing pleural calcification on a film without reason to consider tuberculosis, was proved right in his suggestion that it might be coccidioidal in origin. The fact that these calcifications are not outstandingly frequent in our cases of coccidioidal granuloma indicates that they are not of great significance in judging the likelihood of development of the systemic disease.

These calcifications appear late (21) and can be associated directly with the primary infection only by prolonged progress studies. When calcifications are associated with manifestations otherwise attributable to either a primary tuberculosis or coccidioidomycosis, the question may arise as to which disease occurred first.

During an acute primary attack, the roentgen appearance of the chest may most closely resemble tuberculosis or pneumonia. When adenopathy is not evident, pneumonia is simulated, and the slow resolution may not exclude it. Obvious adenopathy

requires consideration of tuberculosis or the mycosis. Sputum and sensitivity studies are indicated, and progress examination to note the rapidity and completeness of resolution. Residual strand shadows, discrete nodes, and enlargement of the lymph nodes would be significant.

Both tuberculosis and coccidioidomycosis are studied roentgenographically during the primary attack in only a minority of cases. Both are probably typed roentgenographically by cases of exceptional severity. Visible adenopathy, parenchymal lesions comparable in character, and at times erythema nodosum are seen in both. Regression of visible lesions is slower in tuberculosis than in the mycosis. Adenopathy in the adult, though not distinctive, heightens significantly the chance of mycosis.

Erythema nodosum (19) is frequently accompanied by hilar or mediastinal adenopathy. In the present state of knowledge, erythema nodosum may be considered to be a non-specific allergic manifestation, most often of tuberculous origin, but in endemic regions frequently also coccidioidal. It may also be due to other causes. The diagnosis will not rest upon the roentgenogram of the chest or the erythema nodosum itself.

Sarcoidosis, lymphomatoid diseases, and other causes of adenopathy in the thorax may require consideration in comparison with the primary mycosis. These will be considered in relation to the secondary stage of coccidioidomycosis, in which adenopathy constitutes an even more prominent feature.

COCCIDIOIDAL GRANULOMA

After the primary invasion, a number of patients, proportionally small but large in the aggregate, are destined to develop the serious secondary form. The factors of this liability are not yet clear (8). Primary involvement predominates in the female, and appears not to be related to race, social status, or occupation (22). The secondary form shows a marked predilection for Mexicans, Negroes, Filipinos, and Chinese, of male sex, with occupations entailing special contact with soil or its products.

Coccidioidal granuloma may be either an acute progressive disease, fatal in a few weeks or months, or it may be chronic and protracted, with few or isolated foci of infection, ending in apparent recovery or disappearance of the patient from observation in relatively good condition. The chronic type may become acute, but many known fatal cases were acute from the beginning.

Concerning the pathology it is sufficient to say that the secondary stage is essentially granulomatous, with a tendency to abscess formation, while the acute progressive form is especially prone to widespread dissemination. Acute lesions have a predilection for direct invasive spread.

The mortality is customarily stated as 50 per cent. Fifty-six per cent of our patients are known to be dead. Unknown and later deaths will make the actual figure considerably higher. Our mortality, no doubt, is increased by the severe and terminal cases which enter a charity hospital.

Of our 113 cases of coccidioidal granuloma to date, roentgenograms of the chest were made in 99. Most of the remainder were moribund or semi-terminal on admission.

Extrapulmonary manifestations have been present in a large majority of our cases, and add so significantly to the likelihood of the disease that they should be mentioned before describing the pulmonary findings. These include enlargement of superficial lymph nodes, superficial or deep soft-tissue abscesses, granulomatous nodules, ulcers or sinuses from adjacent infection in the skin, meningitis, and lesions of bones and joints. These tend to be multiple. Osseous and articular involvements are particularly suggestive. They have been described (3) and are discussed elsewhere in this symposium.

The chest was persistently negative in only 7 patients, 5 of whom survived. Three apparently recovered; one patient died with bacterial endocarditis, which was presumably the cause of death. Intra-

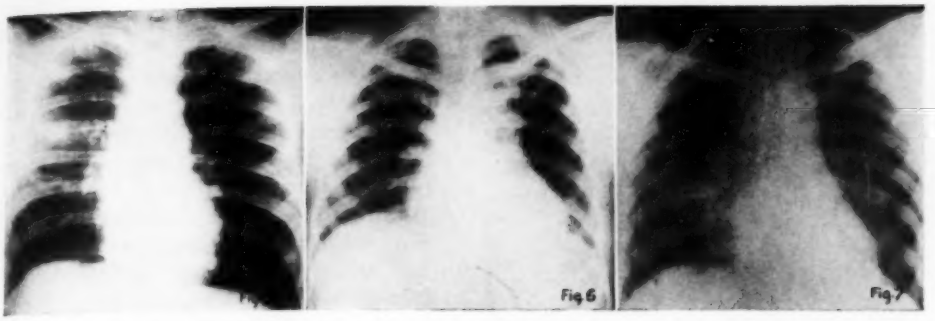

Fig. 5. Coccidioidal granuloma with "mottled" infiltration and mediastinal adenopathy.
Fig. 6. Apical "cloudy" infiltration, local adenopathy, and an associated marginal lesion of a rib.
Fig. 7. Consolidation, adenopathy, obscure miliary involvement, destruction of the inferior angle of a scapula.

thoracic involvement is associated with nearly all fatal cases.

Mediastinal adenopathy is the outstanding and most frequent single manifestation seen on the film (Fig. 5). It was present in 70 of the 92 cases having intrathoracic involvement (77 per cent). This figure is much higher than that originally reported (2), due principally to more assurance in recognizing small enlargements. Most enlargements are rather pronounced, and some are extreme.

Hilar involvement remains a frequent (64 per cent) manifestation, discounting the indefinite "hilar thickening," which is difficult to evaluate, and considering only discrete lymph node enlargements. It is occasionally seen without recognizable mediastinal enlargement but is usually associated with it.

Ten patients had hilar or mediastinal adenopathy alone. Of these, two died: one shortly after examination, with a fine, radiographically invisible miliary involvement, and the other from meningitis, the only intrathoracic involvement found at autopsy being an enlarged hilar lymph node which was recorded on the film. Thus, the great majority of our fatal coccidioidal granulomas have been associated with pulmonary as well as lymph node involvement.

The chests having no evidence of hilar or mediastinal adenopathy were of interest. Only 19 were found, excluding those in which adenopathy was questionable. Seven of these chests were entirely negative; the remainder otherwise displayed characteristics definitely against the predilections of the disease, including the following: 3 had thin-walled cavities associated with fibrotic manifestations at the apices (Fig. 4); 3 had arthritis of synovial origin; 1 had a cyst-like cavity alone; 1 had a pleural lesion alone; 1 had definitely nodular lesions; 1 had discrete miliary involvement. The known mortality was 33 per cent, distinctly less than that for the series as a whole, and only moderately greater than that for patients with entirely negative chests (25 per cent).

Frank parenchymal lesions occur in several forms and are usually associated with some degree of mediastinal or hilar adenopathy. They may occur in any part of the lung and were present, sooner or later, in most of the chests surveyed.

Thickening of the bronchovascular pattern, as distinct from definite parenchymal infiltration, is frequent but difficult to evaluate. It may occur as heavy trunk shadows; less often as an accentuation of the peripheral vascular pattern. No special significance is seen in these manifestations, which are not distinctive; they are usually associated with more significant lesions.

Diffusely scattered, irregular infiltrations, described under such vague terms as "mottling," are common (19 per cent).

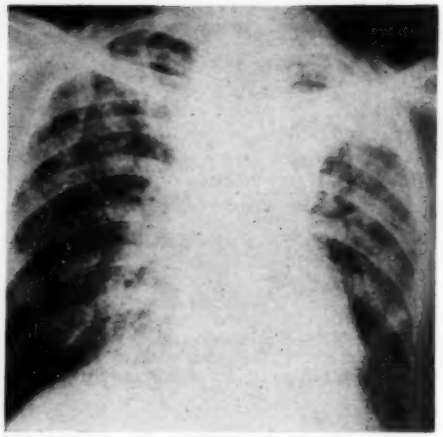

Fig. 8. Coccidioidal granuloma: miliary lesions, exceptionally coarse and discrete.

This entirely non-distinctive manifestation is seen in a wide variety of diseases. It is prone to be less peripherally accentuated than in tuberculosis (Fig. 5).

Indefinite cloudy zones are very frequent (37 per cent) (Fig. 6).

Actual consolidations are fairly common (18 per cent). They are not usually massive or fully lobar and usually appear to be confluences of nodular lesions (Fig. 7). Occasionally they will be seen to contain small acute-appearing cavities, similar to those of tuberculosis, but less frequently evident.

Miliary manifestations are evident in approximately a third of the cases. On the whole these are more indefinite than in tuberculosis, and often amount only to an indefinite ground-glass haze (Fig. 7). The involvement may become almost confluent. As in tuberculosis, the miliary involvement may be invisible. Sharply discrete miliary lesions are relatively infrequent, but accumulating cases are proving them to be less uncommon than was originally thought (Fig. 8). At one time we believed the discrete miliary lesion to be a definite point against coccidioidal granuloma; that can no longer be said.

Scattered coarse nodular or hazy nodal foci were seen in a few cases, but appear to be a minor manifestation in coccidiosis. This picture is particularly tuberculosis-like and is usually seen in the acute disease.

Visible air-containing cavities are relatively infrequent (10 per cent) as compared to tuberculosis of comparable extent. Some are of the small acute type, occurring in zones of partial or complete consolidation, resembling the acute cavities of tuberculosis. Rounded, thin-walled cavities occur, surrounded by infiltration or fibrosis, especially tuberculosis-like. Cyst-like cavities may be surrounded by apparently normal lung and are presumably residual from the pulmonary infection. No large fibrous-walled cavities have been seen in our series. The sparsity of visible cavities is in sharp contrast to the number of excavations noted at autopsy. Apparently bronchial drainage is not readily established.

Fine linear (9 per cent) or coarser strand shadows (14 per cent) of fibrotic appearance were occasionally seen. These were especially prevalent in the chronic cases and may in some instances be residual from the primary invasion (Fig. 9).

Solitary, discrete nodal densities were seen in three cases; in one case this was evidently residual from the original primary attack and in the others may well have been so (Fig. 3).

Pleural exudate is found in about one-fourth of the cases. Usually this is local, plastic-appearing, and adjacent to evident parenchymal lesions or to lesions of ribs or the thoracic wall. Occasionally it is in the form of interlobar strand shadows. Sometimes free pleural exudate occurs without other evidence of thoracic involvement. On the whole, there is less evidence of old, well organized pleural thickening than in tuberculosis.

Lesions accentuated at, or located in, the apices or subapices are found on resurvey to be present more frequently than was originally thought; they were seen in about one-half the cases. These may be of any type—cloudy, mottled, solid, linear, fibrotic, or cavernous. They are especially suggestive of tuberculosis. This was particularly true of three cases having

small cavities and linear manifestations without evident adenopathy. Although in none of these was autopsy proof obtained of the pulmonary lesions, they are now thought to be coccidioidal (Figs. 4 and 6).

Pulmonary manifestations from which descending bronchogenic dissemination would be inferred, or the classical acinous-nodose appearances of tuberculosis, were not seen. Through the courtesy of Dr. Earl Miller of the University of California we have seen one chest whose appearance suggested bronchogenic spread.

An osseous lesion evident on the film of the chest remains a prominent manifestation, and occurs in about one-fourth of the cases. These are seen in ribs, scapulae, clavicles, and spine. Such lesions have been described elsewhere (3) and will be discussed in another paper in this symposium. They add so significantly to the possibility of Coccidioides infection that, with any support otherwise, a provisional diagnosis seems justifiable (Figs. 6 and 7).

Lymph node (9 per cent) or parenchymal (5 per cent) calcifications are not noticeably more frequent than would be true of a similar number of neutral chests from patients of the same class. It is not known how many of these may be residual from the primary coccidioidomycosis. One small pleural calcification was seen.

Combining the above we may recognize several broad types of roentgen appearances in the chests of coccidioidal granuloma.

(1) Adenopathy with any or several of the more active types of pulmonary lesions mentioned. This comprehensive type is the most frequent of all and may be called the "typical coccidioidal chest." It is most commonly associated with the acute disease or more severe subacute or chronic involvements. There are usually associated extrapulmonary lesions which give the clue to the diagnosis.

(2) Adenopathy alone, or associated with inactive appearing manifestations such as linear or strand shadows, discrete nodal foci, calcifications, or pleural thickening. This type is prone to be associated with chronic or non-progressive involvement, particularly isolated or sparse extrapulmonary manifestations: lesions of joint or bone, soft tissue abscess, articular lesions of synovial type, or cutaneous ulcers. It is of interest that such extrapulmonary lesions may be the sole complaint and may develop after a local injury, indicating that a latent infection was readily excited in a site of diminished resistance. Retropharyngeal abscess or peritonsillar infection which may cause cervical spondylitis or cervical node abscess is prone to be associated with such a chest. In cases of this type the prognosis appears better than the average, and there may be apparent recovery or protracted indolent local involvement without generalized spread. The meninges are, of course, a fatal site for isolated metastatic involvement.

Fig. 9. Coccidioidal granuloma: heavy strand shadows. There were several chronic osseous lesions, and a year and a half after the first admission these lesions were apparently healed, and the patient was clinically well. The strand shadow may be residual from the primary infection.

(3) General miliary involvement of the lungs. This is nearly always associated with evident adenopathy, though occasionally not. It invariably leads to early death, and is nearly always present in acute fatal cases. Such involvement can develop rapidly, as it is found at autopsy to a degree calculated to appear on the film, when examination a few weeks preceding

has failed to reveal it. While the disease is usually profusely metastatic when miliary involvement is present, there may be only meningitis and/or inconspicuous lesions otherwise.

In the adult the associated adenopathy would be a non-conclusive point for the mycosis, against tuberculosis. The miliary appearance is not a specific manifestation and requires consideration of numerous possibilities which cannot be elaborated here. Lymphomatoid diseases, sarcoidosis, miscellaneous mycotic infections, silicosis, metastatic neoplasms, and even passive congestion or incidental manifestations of summation of shadows can be responsible.

Tuberculosis: Most of the roentgen appearances described above are compatible with a diagnosis of tuberculosis. The major predilections of the granuloma are minor ones for tuberculosis. Manifestations particularly suggestive of the mycosis are: the adenopathy, with or without the various parenchymal lesions; sparsity of cavities; associated osseous lesions.

The granuloma with meningitis and miliary involvement of the lungs, alone, is particularly apt to be considered tuberculosis. It is more important to be alert to the possibility of mycosis than to attempt to erect points of roentgenologic differentiation. This may lead to sensitivity tests and bacteriologic studies, by which alone a positive diagnosis is made.

The association of pulmonary tuberculosis with extrapulmonary coccidioidomycosis has been particularly confusing. In these few cases the pulmonary involvement followed the major predilections of tuberculosis.

Lymphomatoid Diseases: Vieta and Craver (25) found nothing distinctive between the pulmonary manifestations in the lungs in Hodgkin's disease, lymphosarcoma, and lymphatic leukemia. Mediastinal and hilar enlargements and infiltrative parenchymal lesions were frequent. Discrete nodal densities were rare only in lymphatic leukemia. Pleural thickening and pleural fluid were common. Consolidation may be inferred from such terms as "confluent lobular foci" and "massive lobar infiltration." Hodgkin's disease alone was cited as showing occasional cavities.

These three diseases, like coccidioidal granuloma, have a major predilection for mediastinal and hilar adenopathy and infiltrative parenchymal lesions, and a lesser incidence of pleural involvement and of discrete parenchymal foci. No roentgen point of distinction appears available on the film of the chest for many cases of both conditions. Miliary lesions are uncommon in the lymphomatoid diseases. Osseous lesions are less common in the lymphomatoid diseases and are not infectious in type. Myelogenous leukemia, having no tendency to mediastinal adenopathy, is apt to resemble pulmonary coccidioidomycosis only in occasional cases showing a hilar mass, parenchymal infiltration, or a pleural manifestation. Mycosis fungoides, according to Vieta and Craver, occasionally shows mediastinal adenopathy and frequently infiltration. It may also simulate coccidioidomycosis. Difficulty of differentiating lymphomatoid diseases is most apt to arise early in the study of a case, before the laboratory work appropriate to the two conditions is done.

Pulmonary sarcoidosis (18) may occasionally resemble coccidioidal granuloma. Both may have mediastinal enlargements, with or without miliary lesions, scattered nodular foci, or infiltrations radiating from the hila. Sarcoidosis appears to have a more symmetrical appearance in the two lungs than would be seen, except occasionally, in the mycosis. Sarcoidosis may have cutaneous lesions, from which the diagnosis may be made microscopically, and the clinical symptoms will usually be less severe. While both diseases may have cystic lesions in the bones of hands and feet, those of coccidioidosis will usually show frank evidence of infection, with sinuses, while those of sarcoidosis are indolent and may be clinically silent.

Bronchogenic carcinoma must occasionally be distinguished from coccidioidal granuloma. Either disease may show

enlargement of the lymph nodes and noncharacteristic parenchymal lesions, some of which may be miliary. The pneumonitis or neoplastic consolidations of the carcinoma may resemble the parenchymal lesions of the mycosis. Both may have adenopathy without an obvious parenchymal lesion. Cavities in the carcinoma are usually abscess-like, located in a tumor of the peripheral type, and may have a fluid level. Those of the mycosis are more tuberculosis-like.

Other fungous infections of the lungs, like coccidioidal granuloma, are relatively uncommon, and comparisons by large series, roentgenographically studied, are not usually available. Broad predilections only can be cited. Most mycoses are essentially granulomatous, having a varied tendency to persistent organized lesions: abscess, cavities, fibrosis, metastatic spread, invasiveness, and adenopathy. Some may be either chronic or acute, and some have a special tendency to protracted indolent involvement. As in coccidioidomycosis, one can readily list manifestations of the disease which have occurred. Close differentiation is not available.

Geographic considerations are important. Coccidioidomycosis is prevalent in California, centering about the San Joaquin Valley. Secondary centers occur in Texas, Arizona, and New Mexico. Blastomycosis is prevalent in the central and southern states. Actinomycosis is associated with rural conditions. Climate, and even its yearly variations, are a factor (10, 14, 15).

Blastomycosis is less frequently generalized than coccidioidal granuloma and less prone to profuse metastasis. When this happens, multiple osseous lesions may be found, which are indistinguishable from those due to Coccidioides. Pulmonary involvement includes miliary, nodular, and nodal lesions; confluent infiltrations and consolidations; cavities, air-containing or filled with necrotic material; and fibrosis, which may be diffuse or may occur in sheets, strands, or masses. Adenopathy and organized pleural lesions are common. A characteristic studding along the main vascular trunks has been cited by Brooksher (1). We have not recognized this studding in the few cases seen by us.

In two cases very tuberculosis-like, bilateral, apically accentuated involvement, which became sparser toward the bases, suggested bronchogenic spread. One patient had consolidation in an upper lobe, with an associated destructive focus in an adjacent rib.

Blastomycosis appears to have a greater tendency to fibrosis than coccidioidomycosis, and less to adenopathy and miliary involvement. No absolute roentgenologic distinction appears to be available.

Actinomycosis: The primary infection may be pulmonary, cutaneous, oropharyngeal, or in the digestive tract. About 15 per cent of cases are found to involve the thorax (10). The disease is characterized by marked invasiveness, only moderate metastatic tendencies, fibrosis, and abscess formation. The involvement may be either primary or secondary.

Our cases of actinomycosis with pulmonary involvement, 15 to date, are of the customary types. Several have been "pneumopulmonary," having parenchymal involvement. Most of these have had spreading consolidations, some of which became massive; two had scattered nodal lesions; one had tuberculosis-like, bilateral "cloudy" apical lesions without evident adenopathy, but with foci of infiltration spreading caudally along the lateral peripheral portion of the lung, in a manner unusual for that disease. Several cases have been "pleuropulmonary" with empyema and involvement of the adjacent lung. The lesions of either type tend to burrow invasively into adjacent structures, regardless of their point of origin, involving lung, pleura, mediastinum, pericardium, or the thoracic wall, so that in a late stage the origin may not be determinable.

We have had no typical case of the uncommon "bronchomycotic" type, in which the involvement is confined to bronchi, as occurs in some of the more benign fungous diseases. One patient had widespread marked peribronchial thickening associated

with scattered nodal lesions, which may indicate that metastatic foci of infection were added to a bronchomycotic involvement. Scattered nodal lesions have been classified as metastatic (14).

The predominant invasive spread of pulmonary lesions, and fewer and more massive extrapulmonary manifestations, are against the predilections of both coccidioidosis and tuberculosis. Individual cases resemble either closely.

Moniliasis: Monilia is so commonly a secondary or incidental invader in other diseases, and found so frequently with minor symptoms and radiographic findings, that the diagnosis of clinical moniliasis tends to be controversial. Rigid elimination of other infection, persistence of Monilia in the sputum, and careful prevention of contamination of examined specimens are required. The cases are usually mild, but may be severe and have been fatal.

Roentgen manifestations range from non-distinctive hilar and peribronchial thickenings to extensive infiltrations radiating from the hila; miliary lesions, which tend to be large and discrete (10); scattered, patchy foci; local consolidations; basal consolidations with bronchiectatic cavities. Associated extrapulmonary lesions and metastatic spread are not a feature of this disease. The more common bronchitic type does not usually resemble either tuberculosis or coccidioidomycosis and compares most closely with the benign bronchomycoses.

Pulmonary torulosis is relatively infrequent. Pulmonary lesions of various kinds have occurred, including miliary foci, nodulations, consolidations, abscess, and thickening of peribronchial structures. A terminal meningitis is common. Lymph node enlargements are not frequently mentioned. Fibrosis is common. No characteristic roentgen signs are evident. We have seen one case in which the lung had a discrete area of density comparable to those residual from primary coccidioidomycosis. The active lesion involved the knee.

Streptothricosis: Involvement in the thorax in streptothricosis is usually pulmonary in origin, and the disease may be acute or chronic.

Consolidations, abscess, bronchopneumonia, pleuritis, miliary and nodular lesions, have been found. The disease may resemble tuberculosis or other severe fungous diseases, particularly actinomycosis.

Miscellaneous bronchomycoses, usually chronic, include, among others, infections by Aspergillus, Penicillium and Mucor. Their predilection is to chronic involvement, with interstitial fibrosis, emphysema, bronchiectasis, and peripheral peribronchial abscesses (10). These have been described well by Fawcitt (14, 15). He found a mixture of the three to be associated frequently with exposure to moldy hay; Penicillium especially with moldy grain; and Mucor with exposure to manure and soil.

No detailed description is attempted here because the manifestations, on the whole, are quite different from the diseases we have considered: thickenings of the bronchovascular pattern, emphysema, and in more advanced stages, confluent fibroses and miliary-like stipplings. Fawcitt found that rather acute symptoms might accompany any concentrated inhalation exposure.

COMMENT

Fungous diseases of the lung share with tuberculosis the characteristics to be expected when there is organized cellular response to infection. These include involvement of lymph nodes; persistent parenchymal lesions of many forms, massive, nodular, and miliary; variously appearing diffuse infiltrations, none of which is characteristic of any specific disease. The predilections of these differ somewhat from disease to disease. No attempt has been made to include all possible fungous diseases of the lung in this article.

Those experienced in viewing films of tuberculous patients have erected, from thousands of cases, a conception of typical

forms of tuberculosis. Even the less frequent types are seen so often that other granulomatous diseases of the lung are not likely to present features that we do not recognize as tuberculosis-like.

The fungous diseases are observed in such small numbers that no one person sees sufficient to have met all the varied appearances they may produce on the film.

It is, perhaps, more important to acquire grounds for the suspicion of a fungous disease than to acquire skill in differentiation between them. Once the suspicion is voiced, search for the organism can be made.

It is important to remember fungous diseases when mediastinal involvement is found.

Geographic location is important. Coccidioidal granuloma, for instance, is now kept so constantly in mind by our staff that, as often as not, it is suspected before the first roentgen examination.

1200 N. State St.
Los Angeles, Calif.

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Roentgen Diagnosis of Fungous Infections of the Gastro-Intestinal Tract[1]

ALBERT K. MERCHANT, M.D.
Stockton, Calif.

THE GASTRO-INTESTINAL tract is the site of fungous infections much less frequently than are the lungs or skeletal system. Of the relatively small number of cases in the literature, the great majority are actinomycosis. Blain and Sanford and Voelker estimated that 18 per cent of the cases of actinomycosis reported in the United States up to 1932 were intra-abdominal, involving the appendix, intestine, or liver.

Despite the rather frequent occurrence of buccopharyngeal lesions, reports of actinomycosis of the stomach, duodenum, and jejunum are rare in the literature. It has been suggested that the acid secretions of the stomach may kill the fungus or inhibit its activity, while the fluid contents of the small intestine are not likely to produce abrasions of the mucosa through which the streptothrix might invade the deeper tissues. An attack of appendicitis, however, may give the opportunity for which the organism is waiting, with the result that actinomycosis of the cecum and appendix is relatively common.

In 1928 Sir W. I. de Courcy Wheeler reported a rare case of actinomycosis of the duodenum and jejunum. The patient was a forty-year-old male who had been ill four months with vague abdominal pains and loss of appetite and weight. His temperature had ranged from 99° to 101° during his illness and he had experienced one attack of hematemesis shortly after hospitalization. No hydrochloric acid was found in the gastric contents. The x-ray examination was incomplete (due to inadequate equipment), but the stomach was found to be dilated and hypotonic. There were diffuse narrowing of the pyloric segment and gross irregularities of outline in both curvatures. A large six-hour residue was demonstrated, and the impression gained by the x-ray study was that of pyloric obstruction due to carcinoma. At operation the stomach and first portion of the duodenum were considered normal. A tumor the size of a bantam's egg was found in a loop of jejunum 12 inches from the duodenojejunal juncture. The mass was adherent to the omentum and when the adhesions were freed the isolated tumor appeared red and acutely inflamed on the surface, very similar in appearance to an acutely inflamed appendix before rupture. The loop of jejunum containing the mass was resected but the patient died on the eighth postoperative day. Postmortem examination showed leakage at the site of the anastomosis and a second area of ulceration was found in the third portion of the duodenum similar to the one resected from the jejunum.

Blain reported a case of actinomycosis of the stomach in a thirty-seven-year old male, in 1933. The patient complained of epigastric pain one hour after meals, the pain being relieved by food or baking soda. Roentgen examination revealed a deformity of the stomach which affected the passage of the meal through the pylorus but did not produce obstruction. A diagnosis of chronic gastric ulcer was made. At operation a mass was found on the lesser curvature and posterior wall. Subtotal gastrectomy was performed because the lesion was considered malignant. The gross specimen showed thickening of the gastric wall and the presence of multiple abscesses but no mucosal ulceration. Microscopic studies revealed a chronic granulomatous reaction with dense lymphocytic and plasma-cell infiltration, necrosis, suppuration, and abscess formation. The

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patient recovered from the operation but died several months later because of multiple liver abscesses.

Although actinomycosis of the stomach, duodenum, and jejunum is only rarely encountered, involvement of the cecum and appendix is not infrequent. The characteristic onset is similar to an attack of appendicitis with resultant inflammation and peritonitis. Operation usually reveals a peculiar low-grade productive inflammatory mass in the region of the cecum and appendix, which may or may not be involved in an acute purulent peritoneal reaction as a result of secondary infection following perforation. If the patient recovers from the acute peritoneal incident the course subsequently becomes that of the chronic type, in which the usual progress of the disease, without operation, is from induration to the formation of tumor-like masses with subsequent softening and secondary infection. This results in abscesses with eventual perforation of the abdominal wall and fistula formation. The gradual extension of the processes to neighboring organs and tissues may result in extensive dissecting necrosis or intestinal obstruction because of the dense productive inflammation. Distant metastases sometimes occur as a result of invasion of blood vessels by the organism.

It is hardly possible to make a diagnosis of actinomycosis of the cecum by x-ray, the roentgen findings in these cases being essentially the same as those in tuberculosis or carcinoma. The presence of a sinus or fistulous tract should make one suspect actinomycosis, and the presence of the characteristic "sulphur granules" is of course pathognomonic.

The gastro-intestinal tract appears to be practically immune to blastomycotic infection. Even in the few cases of generalized blastomycosis appearing in the literature, no mention is made of gastro-intestinal involvement by the organism. An unusual case of blastomycosis of the esophagus, however, was reported in 1928 by Vinson, Broders, and Montgomery. The patient came to the Mayo Clinic nine months after discovering some obstruction to the passage of solid food through the upper esophagus. X-ray studies showed a smooth obstruction in the upper esophagus thought to be due to a benign stricture. Esophagoscopy revealed an annular funnel-shaped lesion which was granular and soft. The lumen of the stricture was about 4 mm. in diameter. A piece of tissue was removed for microscopic examination and found to be part of a blastomycotic granuloma.

In 1905 Ophüls proved the fungous nature of coccidioides lesions and commented upon the absence of intestinal involvement in these cases. In an extensive review of the literature and 50 cases of his own, Dr. Ray A. Carter in 1931 concluded that "the gastro-intestinal tract is notably free of lesions." Despite the increasing frequency with which the disease is being recognized in the lungs and skeletal system, coccidioidal involvement of the gastro-intestinal tract is extremely rare. Greaves reported a case with intestinal lesions in 1934. The involvement was generalized, with subcutaneous lesions in the scalp, neck, back, and chest, and intra-abdominal lesions. Smears and cultures from the ulcerated subcutaneous nodules revealed the *Oidium coccidioides*. There were no symptoms referable to the intestinal tract. Postmortem examination showed the parietal peritoneum thickened and adherent to the visceral peritoneum by recently formed gelatinous adhesions. The entire peritoneum was studded with miliary nodules closely resembling miliary tubercles. Similar nodules were present in the heart muscle, spleen, kidneys, and liver. Two intestinal ulcers were found. One of these was in the lower jejunum and the other in the mid-ileum, each of them measuring less than 1.0 cm. in diameter. The margins of the ulcers were yellowish in color, raised above the surface of the surrounding mucosa, forming a halo about the craters.

SUMMARY

1. The digestive system is very rarely involved below the mouth and above the cecum by fungous infections.

2. It is difficult to account for the absence of coccidioidal involvement of the intestinal tract when one considers the many points of similarity between the lesions of coccidiosis and tuberculosis in other parts of the body.

3. There are no known pathognomonic roentgen signs of fungous infections of the gastro-intestinal tract.

Stockton, Calif.

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Coccidioidal Infection in Bone[1]

CARL D. BENNINGHOVEN, M.D.
San Mateo, Calif.
and
EARL R. MILLER, M.D.
Division of Radiology, University of California Medical School, San Francisco, Calif.

DURING THE LAST forty years about 500 cases of coccidioidosis have been reported to the California State Department of Health. Many of these cases are reviewed in Special Bulletin Number 57 from that department.

The disease is produced by the fungus *Oidium coccidioides*, usually found in the soil. The adult form is a spherule 40–50 microns in diameter, having a doubly refractile capsule. It contains endospores which are released by the rupture of the capsule and which become adult spherules. Pathologically, these endospores produce nodules which closely resemble those of tuberculosis. The nodules may caseate or liquefy, producing abscesses. The lesions tend to be progressive and have a marked tendency to dissemination *via* the blood and lymph streams.

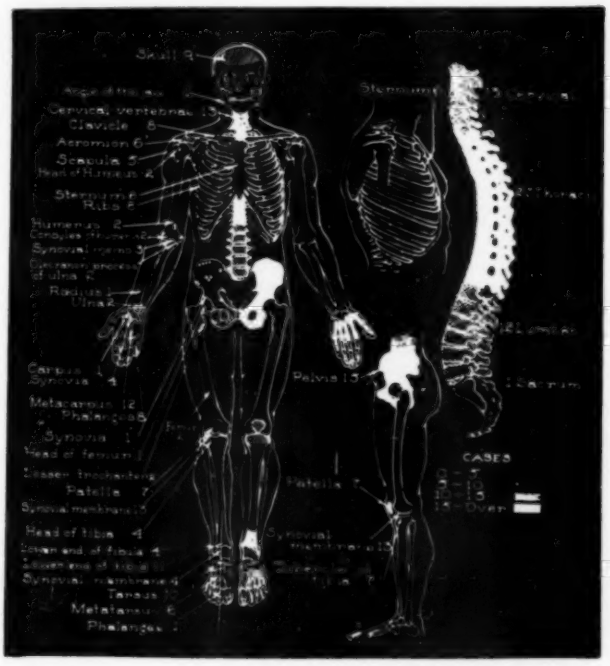

Fig. 1. Distribution in bones and joints of lesions due to Coccidioides. No bones are exempt. The spine, pelvis, and periarticular regions are particularly involved, with special predilection for bony prominences. Diaphyseal lesions are rare except in the short bones of the hands and feet.

The incidence in the male is about four

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Fig. 2. Three rather typical punched-out lesions in the calvarium. One of the lesions particularly shows the tendency for the outer table to be involved to a greater extent than the inner table. There is practically no bone reaction around the lesion.

times that in the female. Occupations where contact with the soil is close, such as ranching and fruit picking, account for most of the cases and explain the sex distribution. Most cases originate in the middle and southern parts of California.

The disease has a primary and a secondary phase. The portal of entry for the primary infection is the respiratory tract. This phase resembles a mild influenza clinically and commonly is diagnosed as "valley fever" because of its frequent appearance and recognition in the San Joaquin Valley. It may or may not be associated with erythema nodosum. The chest film shows a small pneumonic focus with hilar adenopathy resembling that of the primary phase of tuberculosis. This primary infection induces an allergic state which is demonstrated by a positive skin response to coccidioidin. All patients recover from the primary infection within a period of a few weeks.

Once the allergic state is established, re-infection endogenously or through the respiratory tract or skin, may induce the disease in its secondary or chronic granulomatous phase. In only a small percentage of those having had the primary infection does the secondary phase develop. After a secondary focus is established in either lung or skin, the disease becomes progressive, with varying periods of latency, sometimes of years' duration. Metastatic foci in the soft tissues, bones, and parenchymal organs ultimately appear. Miliary dissemination is the terminal manifestation.

In bone there are several commonly encountered types of lesions.

Fig. 3. The multicystic lesion with trabeculae of bone between the areas of destruction, a lack of any significant reaction of the surrounding bone, and erosion of the lesion through the margin of the bone is not infrequently encountered, especially in the flat bones. There is an associated soft-tissue abscess.

1. Uniloculated or Multiloculated Cyst-like Areas: In this type of lesion there may be bone expansion with little or no surrounding reaction. Usually there are rather sharply defined heavy strands of bone between the cyst-like areas of destruction.

2. Marginal Erosion: This may be of two forms: a sharply scooped-out area of destruction or an irregularly destroyed area of cortex with surrounding periosteal new bone formation. These areas usually have a reaction wall at the base of the lesion. There is always a soft-tissue abscess at the site, and the latter frequently shows calcification.

3. Destruction with Periosteal New Bone Formation: This type of lesion is a more advanced stage of either of the two just described, and is the most frequent late lesion. There are cancellous and cortical destruction, usually considerable irregular periosteal new bone, a surrounding soft-tissue infection, and rarely sequestration.

Figures 4–6

Fig. 4 shows three rather characteristic separate lesions, any one of which can occur independently. The lesion in the tibial tubercle shows deep destruction and marginal erosion with a soft-tissue abscess and sequestration. This lesion is quite far advanced and because of its position is quite characteristic of coccidiosis. There is an associated synovial infection with a great deal of swelling of the joint capsule. This may be seen alone, *i.e.*, without either bone or cartilage destruction discernible on the films. The periosteal elevation on the anterior surface of the patella is occasionally seen as a separate lesion.

Fig. 5. Diaphyseal destruction with periosteal new bone formation and soft-tissue swelling with calcification is a fairly typical appearance for the infection in the short bones of the hands and feet. Rarely this type of lesion is seen in the long tubular bones.

Fig. 6. Coccidiosis frequently mimics tuberculosis, especially in the spine, where the lesion may be indistinguishable from a Pott's disease, and occasionally in other joints such as this knee, which demonstrates marked erosion of the non-weight-bearing portions of the joint associated with great soft-tissue swelling.

4. Lesions Resembling Osteomyelitis: This type is most frequently seen in the short bones of the hands and feet. Very occasionally the lesion is in the shaft of a long bone, showing widespread destruction and reaction throughout the diaphysis, with surrounding periosteal new bone formation. There is no sequestration.

5. Joint Involvement: Joint involvement may be of two distinctly different types: (*a*) purely synovial, (*b*) synovial with subarticular destruction indistinguishable from tuberculosis. Usually synovial involvement is seen as a large swelling of the joint capsule. Occasionally there is periosteal new bone formation on adjacent bone. This is thought to be a reactive rather than an infective process.

In the lesions which are indistinguishable from tuberculosis there is capsular swelling, marked periarticular osteoporosis, with cartilage and subarticular destruction of bone on both sides of a joint.

Investigation of any advanced case as a rule discloses involvement of several bones and lesions of several types. Sequestration, which occurs rarely, is usually seen in a lesion with cortical destruction and surrounding soft-tissue abscess.

Multiplicity of lesions is the rule. One mandibular lesion is the only known involvement of the facial bones. All other bones have been known to be infected. The bones most frequently involved are those of the spine, pelvis, hands, feet, and the bones adjacent to the knee and ankle.

In the flat bones the lesions may be central or marginal. In the spine, a single lesion may be central but most of the lesions are marginal because of extension of the infection into bone from long paravertebral abscesses. In the long bones the lesions tend to be metaphyseal. The present series, however, shows a number of diaphyseal involvements. In the short bones of the hands and feet, diaphyseal involvement is the rule. Dr. Ray Carter's observation of the predilection of the le-

sions for bony prominences has been borne out in this series.

The epiphyseal cartilage does not act as a barrier to the spread of the infection. It is not unusual for a deep lesion in bone to remain close to a joint without giving roentgen evidence of joint cartilage involvement. Synovial infection may remain limited to the synovia. Occasionally, however, widespread subarticular bony destruction is observed in cases with joint involvement. These probably take origin in bone.

Soft-tissue abscesses are common. They may arise as primary lesions without bone involvement; they may extend to the underlying bone, where they produce marginal erosion and progressive deep destruction; or they may be the extension of a purely destructive lesion in the cancellous bone which has eroded through the cortex.

The prognosis of the disease in its secondary phase is grave. The mortality approximates 60 per cent.

Acknowledgment: Through the courtesy of Dr. Ray Carter at the Los Angeles County Hospital, we were allowed to study the 125 cases recorded there. We wish to express our deep appreciation for Dr. Carter's helpful suggestions. We are grateful, also, to Dr. Smith of the Kern County Hospital and Dr. Newell of Stanford Hospital for allowing us to study their cases.

95 S. El Camino Real
San Mateo, Calif.

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DISCUSSION OF SYMPOSIUM ON FUNGOUS INFECTIONS

(Papers by C. E. Smith; Robert A. Powers;[1] R. A. Carter; A. K. Merchant; C. D. Benninghoven and E. R. Miller)

Philip H. Pierson, M.D.[2] (San Francisco): Fungous diseases of the chest and lungs are so readily recognized today that we hear even our students mentioning these conditions more frequently than a few years ago.

The roentgenologist has a large field to cover. He must be familiar with all phases of medicine. He can describe shadows, but only as he correlates all features of a case, can he see the etiology in those shadows. He is a consultant—a part of a team—

[1] Published in Radiology **37:** 448–453, October 1941.

[2] In the course of his discussion Dr. Pierson showed a series of films of coccidiosis and other chest conditions, with appropriate comments.

and he must have all the information the clinicians can give him in order that his interpretation of the shadows may be of aid in the clinical evaluation of a condition.

Coccidioidal granuloma is said to be relatively rare in the San Joaquin Valley. But let a person go into that area who has not been infected in childhood, and he may have not only a primary lesion but a progressive one. May not this be the same thing that happens when tuberculosis develops in the adult? Many such cases, as is well known, go on to the reinfection stage. Similarly reinfection may account for some granulomas.

The spread of tuberculosis is by direct contact. We say that one person cannot infect another with Coccidioides, but if someone is coughing and expectorating the organisms, and these dry on the floor or furniture, there is no reason why the mycelium, which is responsible for the infection in man, may not easily be passed about. I believe we should not lightly dismiss the infectiousness of coccidiosis just because the actual agent is not transmitted from person to person.

In closing I would like to mention the chest surveys which are now being carried on in different localities, not only by tuberculosis associations but by hospitals as well. If through these surveys we can pick up early fungous disease as well as tuberculous lesions, not only will our knowledge be increased, but we will be helped in preventing the progress of the condition to reinfection and further to the stage of systemic disease.

Frederick H. Rodenbaugh, M.D. (San Francisco): I can recall the earlier days of roentgenology when practically all we saw of coccidiosis were the terminal bone lesions, which had the appearance of any destructive bone lesion and were generally attributed to tuberculosis. Then, beginning some fifteen years ago, an occasional case was seen that did not prove fatal, and gradually with demonstration by x-ray of relatively small pulmonary lesions this formerly unrecognized disease entered into our clinical consciousness. It would seem to me that we are likely to see an increasing number of these fungous infections of the lung in any large group of subclinical cases. We may well find that there is an arrested stage, or stage of relative non-infectiousness.

A larger number of cases have, I believe, come from the San Joaquin Valley than anywhere else, but that, of course, is a populous and highly cultivated region. The next largest group comes from San Benito County, and the next from Arizona. The probability is that the disease exists to a much greater degree in the Middle West than has yet been recognized. A number of years ago some of our Chicago colleagues showed us some remarkable mycotic infections of the lung which were at that time being confused with tuberculosis. I am certain that in my earlier years we called such cases subclinical tuberculosis, though actually they were not tuberculosis at all.

Carl D. Benninghoven, M.D.: Diagnosing coccidiosis of bone from roentgen films alone is very difficult, nearly impossible. A few years back, as a practising radiologist in the San Joaquin Valley, I found the history of great assistance in the presence of a questionable lesion. It is important to know, for example, that the patient is a farm worker, a Filipino, Negro, or Mexican. Race, however, is not too significant, as the disease is found among many of the white people living in the Valley.

We are helped, also, in the diagnosis by finding multiple lesions, sometimes associated with soft-tissue abscesses. The abscesses are filled with a rather characteristic purulent material, in which *Coccidioides immitis* can be demonstrated. Occasionally skin lesions are seen. These are fairly typical and help the radiologist in making up his mind regarding a bone lesion demonstrated on a roentgen film.

The question of cure is difficult to answer. Sixty per cent mortality is given for the secondary stage. It may be even higher than this, as there are many temporary cures with later recurrences. One patient we saw had several recurrences over a period of sixteen years before dying of the disease.

L. Henry Garland (San Francisco): I understood Dr. Miller, in speaking of reinfection, to imply that this is exogenous in character, whereas Dr. Smith stated that exogenous reinfection does not occur in coccidiosis but that the problem is one solely of endogenous reinfection. I wish he would tell me how, ten years after an apparent cure, these organisms can escape from the calcified foci.

Dr. Smith: I must arise under Dr. Garland's stimulation and differ from Dr. Miller on a few points. On the basis of evidence already indicated in the body of my paper, we feel very definitely that reinfection is not from without but from within. In line with that concept, which Dr. Pierson emphasized in connection with tuberculosis, we believe that generally reinfection from within occurs not in an old infection after the organisms have become calcified, but relatively early after the primary infection. In coccidiosis only rarely does dissemination (coccidioidal granuloma) occur after a number of years, though it is true that some cases with long intervals appear in the literature. One example is that of a man who lived in Taft, on the west side of the San Joaquin Valley, and subsequently became a sailor. Ten or twelve years after he left Taft a lesion developed in one knee, which proved to be coccidioidal. This, however, is the exception proving the rule. Generally the patient goes from his primary infection into granuloma (disseminated infection), and it is hard to say where primary infection ends and reinfection begins. An interesting

example is a patient of Drs. Waring and Clark of the University of Colorado Medical School. I hope that they will report this case, which was diagnosed through the alertness of Miss O'Toole of the same institution. We were privileged to confirm their diagnosis and were very excited at the prospect of a case from a new endemic area. They wrote us, however, that the patient gave a history of having been in Fresno County in May of 1940, where he worked for a month on a ranch. Four months later he had his first abscess, followed by many others. He denied that he had any sort of respiratory symptoms while in California. His primary infection was entirely subclinical. In this instance exogenous reinfection was ruled out. Also the time between the primary infection and the endogenous reinfection or dissemination was relatively short.

The association of coccidioidal granuloma with soil exposure, as suggested by Dr. Miller, is not so simple. Coccidioidal granuloma does occur predominantly in males, more than 4 to 1, and this might be explained on the basis of occupational exposure. However, erythema nodosum caused by *Coccidioides* occurs more frequently in females. Among 432 patients with erythema nodosum due to *Coccidioides* seen in Kern and Tulare Counties during a year and a half, the females outnumbered the males better than 2 to 1. Coccidioidin tests in the Kern County schools in association with Doctor Myrnie Gifford and others of the Kern County Health Department indicated an equal distribution of infection between the sexes. All we can say is that while there is no sex difference in infection, males are apparently more prone to develop coccidioidal granuloma and females to have erythema nodosum. It will be recalled that primary infection with erythema nodosum only rarely goes on into coccidioidal granuloma.

Race also enters the picture. This is not a matter of difference in exposure to soil. Dr. Gifford's studies in Kern County have demonstrated a coccidioidal granuloma death rate among Negroes 23 times that for the whites and among Filipinos 170 times the rate for whites. Drs. Carter and Kessell have observed in the Los Angeles General Hospital that Filipinos, Negroes, and Mexicans constitute a disproportionate percentage of the granuloma patients. Of our 432 valley fever patients, however, none was a Negro, only 2 were Filipinos, and 2 orientals. These conflicting data would seem to eliminate exposure to soil, *per se*, as the cause of coccidioidal granuloma, *i.e.*, dissemination in the human host.

As to the distribution of *Coccidioides*, that is a subject for which there is insufficient time. The same is true of diagnosis and the significance of the coccidioidin test. A negative skin test followed by a positive skin test is diagnostic. A positive test alone would not be diagnostic even though the roentgenographic appearance were compatible. Preferably, one would wish to recover the fungus. Seeing something suspicious in the fresh coverslip preparation is not sufficient. Fat droplets and other artefacts are very hard to differentiate from *Coccidioides* in sputum specimens and the odd organism in a specimen of pus. To be certain, one should end with a culture in the test tube, and animal inoculation followed by the development of double-contoured spherules with endospores. In tissue sections the situation is quite different. There, if double-contoured spherules with endospores and without budding are observed, one can be sure of the diagnosis. Additional procedures may assist in evaluating the significance of the positive coccidioidin test. The sedimentation rate, white blood count, and serological tests are of considerable assistance. Unfortunately the diagnosis of coccidioidal infection requires a paper in itself; indeed, a series of papers.

Dr. Miller: It is true, as has been suggested, that these are nondescript lesions. When we see a lesion in the bone, especially in the pelvis, such as I have shown, I think we might suggest coccidiosis first. But in the chest we would have no hesitation in suggesting, for instance, tuberculosis, and on the basis of probabilities this would be a fairly good bet.

So far as reinfection is concerned, it is quite true that endogenous infection is perfectly possible and has been shown to occur. Yet in those persons who have had a primary infection and are being continually exposed to Coccidioides it would be difficult to prove that reinfection was not from the outside. Suppose the infection is endogenous! If it lies quiescent in an individual, he may be considered unaffected as far as the fungous element is concerned. Later the lesion can break down, as in tuberculosis, and the active secondary phase of the disease develops.

Dr. Carter: In regard to endogenous *versus* exogenous infection, those who have had primary coccidioidomycosis are vulnerable, because minor injuries, such as a bumped finger, can start the secondary coccidioidal granuloma. One puzzle is why these isolated foci seem not so very ominous. In regard to the predilection to secondary coccidioidal granuloma, are not the dark-skinned races, mentioned as liable to the granuloma, also prone to adenopathy when they develop tuberculosis? Those patients with the primary disease who show adenop athy seem most apt to have the secondary manifestations. Those having primary cyst-like cavities do not often have much adenopathy and very seldom develop the secondary granuloma.

The Clinico-Anatomical Aspects of the Lumbosacral Region[1]

VERNE T. INMAN, M.D., Ph.D., and JOHN B. deC. M. SAUNDERS, M.B., Ch.B., F.R.C.S.
San Francisco, Calif.

THE PROBLEM OF low back pain with sciatic radiation continues to present many puzzling features, which are reflected by the uncertainty in differential diagnosis and by the multiplicity of procedures which have been advocated for its treatment. The contributions of Mixter and Barr on the intervertebral disc as an etiologic agent constitute a major advance. Nonetheless the enthusiasm engendered by popularization of posterior herniations of the disc as the cause of sciatica has proved too sanguine. The problem is a good deal too complex to be explained by purely mechanistic concepts of pressure on the spinal roots. This is evidenced by the disappointments which have so often followed surgical intervention with this concept solely in mind. On the other hand, in the great majority of cases, sciatica is but a subjective complaint which for the most part is unaccompanied by objective signs. It is now generally accepted that the etiology of this syndrome is extremely varied, being related to congenital, traumatic, infectious, postural, and other agents. Here, too, the greatest difficulty is encountered in establishing the relationship of the lesion to the sciatic radiation of pain.

It seems to us necessary to draw a sharp distinction between the sciatica resulting from root compression, which is essentially a radiculitis, and the sciatica encountered as a vague, infragluteal subjective complaint.

The use of the term sciatica to cover both of these conditions has been responsible for a great deal of confusion, a confusion often compounded in that both may exist in one and the same patient. We feel that the term sciatica has been too loosely employed, concealing, by the very indefiniteness and obscurity of its meaning, all sorts of etiological fantasies. The view that the term implies some association with the sciatic nerve is now a commonplace, and yet, as Schmitter has pointed out, "the word sciatica used in the sense of a nerve affection is an historical impropriety." Because of the lack of precision surrounding the use of the word sciatica, we find it better to avoid the term when possible.

Our purpose in this communication is to discuss certain functional features of the lumbar column in relationship to spinal injury and the question of the mechanism of the infragluteal radiation of pain with which it is so commonly associated. In addition, we propose to describe the relationships of the lumbar and sacral nerve roots in those parts of their course where they are vulnerable to compression and irritation resulting in a lumbar or sacral radiculitis, and further to point out the lack of harmony between the known physiological response of peripheral nerves to compression and the clinical findings encountered in disc and ligamentum flavum injuries. Such a study may help to clarify some of the issues, giving a better understanding of the possible factors involved in the production of the syndrome. These features, we feel, will not be without interest to the radiologist, who is so often called in consultation over these difficult and often puzzling cases.

ANATOMY

The interval between contiguous vertebral bodies is occupied by the intervertebral disc, the vertical thickness of which varies in different parts of the column. The discs, thinnest from the third to the

[1] From the Division of Anatomy and the Department of Orthopaedic Surgery (Division of Surgery), University of California Medical School, San Francisco. Presented before the Radiological Society of North America, at the Twenty-seventh Annual Meeting, San Francisco, Calif., Dec. 1–5, 1941.

seventh thoracic segments, are thickest in the lumbar region. In both lumbar and cervical regions, each disc is somewhat thicker anteriorly than posteriorly, thus assisting in the production of the anterior convexities characteristic of the regional curvatures of these segments of the spine. In the thoracic region the converse occurs, in correspondence with its anterior concavity. Apart from variations in detail, the anatomy of each intervertebral disc is essentially the same.

Three elements make up the individual disc. The first is a circumferential portion consisting of a series of concentric fibrous lamellae and variously known as the annulus lamellosus or fibrosus. The arrangement of the individual fibers is not truly circumferential, for they pass from vertebra to vertebra in an oblique or spiral course to sink into the bone as the so-called fibers of Sharpey, through which the disc obtains its solidity of anchorage. The annulus is supported in front and behind by the anterior and posterior longitudinal ligaments, respectively. The anterior is the more substantial of these ligaments, for the posterior often displays deficiencies where it is related to the disc. It is important to note that posterolaterally, on either side where the annulus comes into relationship with the intervertebral foramen, it is unsupported by any extrinsic ligamentous structure. In these regions, especially in the lumbar column, the disc bulges backward to occupy a considerable portion of the lower half of the foramen.

The second element of the disc is its soft, pulpy, elastic center, known as the nucleus pulposus. This pulpy center is of peculiar functional significance, possessing in health a considerable inherent turgor and elasticity, through which properties it serves to distribute pressure over the vertebral body. It can best be likened to an elastic ball bearing, changing in shape and position under functional demands and so distributing and absorbing the mechanical shocks to which the spine is continually subjected. In the lumbar region the nucleus is large and lies a little dorsal to the center of the disc. In flexion of this portion of the spine it tends to move in a still more dorsal direction.

The third element of the disc is the cartilage plates which bound the disc above and below and cover the bearing surfaces of the contiguous vertebrae. These plates, analogous in a way to the articular cartilages of other bones, are, however, an integral and intimate part of the disc, confining it above and below.

Textbook descriptions of the ligamenta flava are entirely inadequate for a precise understanding of the manner and results of its injury. Consisting predominantly of yellow elastic tissue, they join together the adjacent laminae and articular processes. Whereas the ligamentum flavum is a continuous structure, it is convenient for both descriptive and clinical purposes to subdivide it into two portions. The medial half, the broader and thicker part of the ligament, unites the contiguous laminae and may with advantage be called the interlaminar portion. The lateral half is thinner and is related to the interarticular joint, where it is intimately blended with the capsule. The division is further suggested by the direction of the fascicules of the two parts. The fibers of the interlaminar part are vertically disposed, whereas those of the capsular portion course obliquely downward and laterally.

The inferior attachment of the interlaminar portion is to a well defined groove on the upper border of the laminae below. Sharp, thin plaques or spicules of bone commonly extend up from the anterior crest of this groove into the substance of the ligament. These plaques must necessarily be fractured from their attachment on surgical removal of the ligament and have erroneously been regarded by some as evidence of pathological change in this structure.

An extensive irregular rough area, occupying approximately the lower half of the lamina above, gives attachment to the interlaminar portion, superiorly. This area is separated from the smooth upper half of the lamina by a sharp ridge which

characteristically exhibits a small bony spicule at the junction of the interlaminar and capsular moieties of the ligament. Bony extensions into the ligament as found below have not normally been observed at this attachment.

The arrangement of the ligament is such that the lower half of the spinal lamina is excluded from the neural canal. The medial extremity of the ligament blends with its fellow of the opposite side in the mid-line at the base of the spinous process. Laterally each is continuous with and inseparable from the capsular extension, the transition being indicated by the change in the direction of the fibers.

The capsular element is attached below to a groove which extends along the periphery of the inferior articular process to a point a little beyond the intervertebral foramen. Above, the ligament is fixed to the inferior border of the pedicle and lies just below the groove for the spinal nerve. Laterally, considerably attenuated, the ligament blends with and in part constitutes the anterior capsule of the interarticular joint, some little distance lateral to the intervertebral foramen.

Other related fascial and ligamentous structures associated with the spine of the lumbar and lumbosacral regions are the supraspinous, interspinous, intertransverse, iliolumbar, superficial and deep posterior sacro-iliac, interosseous, sacrospinous and sacrotuberous ligaments together with such fasciae as the lumbodorsal and the aponeurotic extensions from the neighboring muscles. The approximate position and attachments of these structures are sufficiently well known as scarcely to warrant description here.

MECHANISMS OF LIGAMENTOUS INJURY

The relatively violent forces to which the spinal column is subjected during everyday activities are perhaps not sufficiently appreciated. The maintenance of the integrity of the column depends in part on its unique spring-like mechanism for dispersing such forces and its state of internal equilibrium, which in addition counteracts forces of deformation. This equilibrium is established by two forces necessarily equal, but acting in opposite directions. One of these forces is expansile and tends to separate the vertebral bodies. It depends upon the turgor of the intervertebral discs. This force has been experimentally ascertained in the cadaver, by Petter, to approximate 30 pounds in the individual discs of the lumbar region. The other force is tensile and resists separation of the vertebral bodies. It depends upon the various ligaments, such as the annulus lamellosus, the anterior and posterior longitudinal, the interspinous, the supraspinous, and intertransverse ligaments. The elastic nature of these forces permits of spinal movements. When these forces are liberated by separation of the neural arches from the bodies, the expansile force residing in the nucleus pulposus elongates the anterior part of the column while the tensile force of the various ligaments of the neural arches shortens the posterior portion. The change approximates 10 per cent of the total length of the column. These intrinsic forces, together with the primary and secondary curves, give to the column its extraordinary resiliency.

Under functional stress, the pressure exerted upon and distributed through the lumbar vertebrae and intervertebral discs must be enormous. They must, of course, carry the superincumbent body weight. Furthermore, in weight lifting, the lumbar region carries the brunt of the pressure attendant upon use of the spinal column as a lever of the third class. We have estimated, by analysis of the force vectors resultant upon the lower lumbar discs in lifting a weight of 50 pounds, that this pressure amounts, under average conditions, to about 500 pounds. Under other conditions, there are fleeting periods during motion in which the pressure is considerably in excess of this rough estimate. In addition, when the spine is flexed, the nucleus pulposus in the lumbar region migrates dorsally, tension is thrown upon the posterior portion of the annulus, and if some rotation should accompany flexion,

the annulus is further subject to torsional stresses. The magnitude of these forces, the dorsal migration of the nucleus, the stresses thrown upon the posterior part of the annulus, no doubt account for the greater frequency of dorsal herniations in the lower lumbar region. These are sufficient to account for herniation, in a normal disc, from a single trauma. In others, repeated traumata of the discs with attendant weakening of the annulus, or in those with such degenerative changes as we have often observed, these forces alone would serve as an adequate cause of herniation. It should be further noted that, in the act of reaching forward to one side, the anatomical arrangement in the lumbar region is such as to limit that rotation which so freely occurs in the thoracic segments. This limitation forces lateral bending in the lumbar region, which puts the major stress on the posterolateral portion of the annulus and ligamentum flavum of the contralateral side. Such a mechanism would readily account for the unilaterality of lesions of one or both of these structures occurring in the neighborhood of the intervertebral foramen and involving, in the case of the ligamentum flavum, its capsular portion.

It is many years since Virchow demonstrated that, in flexion of the spine, the lumbar region contributes very little to the movements except that the curve is obliterated and the segment becomes straight. This limitation of movement is in contrast to that which occurs in extension. Phylogenetic history in the adoption of the orthograde position evidences the enormous development of the sacrospinal muscles necessary for the maintenance of the erect posture. These muscles have their *point d'appui* on the lower thoracic cage and thoracic spine. They play over, rather than on, the lumbar segments. The lumbar spine may be regarded, in consequence, as a single lever. It is apparent that, should this part of the vertebral column develop an anterior concavity, the tendency would be for the sacrospinalis muscle to approach the axis of the lumbar spine. Such an approach would place the muscle in a position of mechanical disadvantage for protection of the spine, or for recovery from the hyperflexed position. The difficulty of lifting a heavy weight with the fully flexed spine is a familiar observation. Likewise when the spine is forced into hyperflexion its integrity is no longer fully guarded by the musculature, and strain is thrown upon the dorsal ligaments and ligamentun flavum, notably the interlaminar portion. Such a mechanism sufficiently explains injuries to the ligamentum flavum. The association of lateral bending with forward flexion in producing unilateral lesions has already been discussed.

It has been pointed out that structurally the ligamentum flavum consists predominantly of elastic tissue and is normally under tension. When it is torn or injured, its fibers retract. Healing occurs by scar formation. That such scars should undergo hypertrophy is not surprising. Numerous examples of such hypertrophies can be observed in other situations. They characteristically occur in regions where movement is unavoidable and free, as on certain parts of the abdominal wall and in the neck. The persistent stimulation of healing wounds results in excess of fibrous connective tissue, and the hypertrophy is greatest where movement is most. Greig pointed out that such hypertrophied scars are not true keloids but a local response to stimulation, and that they are merely hypertrophied cicatrices. Once injury and scar formation occur in the ligamentum flavum, there can be no question that the factor of movement is continually operative, resulting in hypertrophy of the cicatrix. These conclusions are confirmed by the appearances of every example of hypertrophy of the ligamentum we have been able to examine histologically.

It should not be forgotten that before the disc or ligamentum flavum is involved forced lateral bending must stretch the intertransverse or iliolumbar ligaments, and hyperflexion damage the supraspinous and interspinous, together with related

fascial and aponeurotic attachments. When torsional stress is added, a combined lesion of both lateral and posterior structures is not unlikely to occur.

LUMBAR AND SACRAL NERVE ROOTS

The anatomical relationships of the lumbar and sacral nerves as they lie in the intervertebral foramina are of particular clinical significance. The intervertebral foramina of the lumbar region are formed by the juxtaposition of the deep inferior vertebral notch and the shallow superior vertebral notch of the subjacent vertebra. The shape of the foramen, as seen in the lateral roentgenogram, is that of an inverted pear. This description, while true for the upper lumbar, does not hold for the fifth lumbar foramen. Here the inferior vertebral notch encroaches upon the body of the fifth lumbar vertebra to a depth of several millimeters, and this foramen is directed anterolaterally rather than directly laterally. Because of this arrangement, the fifth lumbar intervertebral foramen is obscured in a true lateral roentgenogram of the spine and appears relatively smaller than is actually the case.

The fibers of the cauda equina, which separate to form each lumbar nerve, leave the dural sac at approximately the level of the intervertebral disc of the segment immediately above. The nerves cannot truly be said to penetrate the dura but carry with them a covering of dura which blends imperceptibly with the epineurium more distally. This contribution of the dura to the connective tissue of the nerve root increases its diameter in the foramen to twice the size within the subarachnoid space. Each nerve is firmly attached to the dura and traction upon the nerve will produce deformation of the dural sac without transmission of the tension to the fibers of the cauda equina. The nerve as it lies in the intervertebral foramen is relatively free, being attached to the surrounding skeletal structures only by fine areolar tissue. As the spinal nerve passes through its foramen, it is closely applied to the medial and inferior surface of the pedicle, occupying a smooth groove on this aspect of the pedicle, known as the sulcus nervi spinalis. At the fifth lumbar foramen, and to a lesser extent at the fourth, the sulcus extends obliquely forward into the body of the vertebra. Attention should be called to the fact that the nerve in its course through the foramen occupies only its upper half, the lower half being more or less occluded by the posterior projection of the intervertebral disc and the anterior bulging of the ligamentum flavum. *The spinal nerve comes in contact with its own intervertebral disc only at its point of emergence from the intervertebral foramen.*

The dural sac, as mentioned previously, lies free in the vertebral canal but is firmly adherent to each segmental nerve as it passes through the intervertebral foramen. At its cephalic end the dura fuses with the periosteum around the foramen magnum. The caudal end is held opposite the third sacral vertebra by a continuation of the filum terminale, which fuses with the fascia over the dorsum of the coccyx.

The vertebral canal lies posterior to the center of motion of each vertebral segment. Because of this relationship, it is apparent that flexion of the spinal column leads to elongation of the vertebral canal, while extension produces shortening. The total change in length of the canal in the range from full flexion to complete extension is approximately 7 cm. As the dural sac is firmly held at both of its extremities, it must in consequence undergo stretching on flexion of the spine. This effect has been studied in cadavers, and the stretching of the dura is rendered apparent by the development in it of longitudinal wrinkles and by the cephalic migration of the dural cuffs formed at the point of emergence of each spinal nerve. As one would anticipate, maximum stretching is seen at the mid portion of the dural sac. Because of the firm attachment of the dura to each spinal nerve, the movement of the dura is directly transmitted to the spinal nerves themselves. In cadavers, flexion of the spinal column causes traction on the dural sac and upward movement

of the spinal nerves. This movement is most marked in the upper lumbar nerves. The first and second lumbar nerves show the greatest upward excursion within the intervertebral foramina, amounting in full flexion to from 2 to 5 mm. The extent of this excursion decreases in the lower lumbar nerves, being just detectable in the fourth lumbar and not appreciable in the fifth lumbar nerve. It may be stated then that with flexion and extension of the spine there is a small but definite piston-like movement of the upper lumbar nerves in and out of the intervertebral foramina.

Lateral flexion of the spine does not produce movement of the contralateral segmental nerves unless the movement is carried to such a degree that tilting of the pelvis and adduction of the contralateral leg occur. In such a position the nerves are made taut, with detectable motion in some cadavers.

The straight leg-raising test has been said to produce traction upon the sciatic nerve. The degree to which such traction would affect the contributing segmental nerves, as they lie in their respective intervertebral foramina, was investigated in cadavers. Pins were inserted into the lower lumbar and sacral nerves as they emerged from their foramina, and to mark the position of the pins in relation to the skeleton, small steel nails were driven into the bodies of the vertebrae at points opposite the pins in the nerves. Straight leg raising was performed and the distance between the nails in the vertebrae and the pins in the nerves was measured. In all cases traction upon the sciatic nerve is demonstrable when the leg is elevated but 15° to 30° from the table. Tension upon the sciatic nerve is transmitted through the plexus and early affects the contributing segmental nerves. Straight leg raising causes a distal migration of the nerve root in the spinal foramen, but this distal migration is never noted at the third lumbar nerve or at any of those above. In some cadavers it is just noticeable at the fourth lumbar. The maximum motion occurs at the fifth lumbar and upper two sacral nerves. The motion in these segments is considerable, being greatest from 60° to 80° of flexion, when the nerves show a total migration of from 2 mm. to 5 mm. In all cadavers some motion of the fifth lumbar and first and second sacral nerve roots in and out of the intervertebral foramina is produced. The maximal motion recorded was 7 mm.

The normal movement of the lumbar and sacral nerves in their respective foramina accompanying the ordinary motions of the spine and hip is of clinical significance. Flexion of the spine produces changing relationships of the upper lumbar nerves, while straight leg raising does the same for the nerves below the fourth lumbar. This suggests the possibility of utilizing spinal flexion and straight leg raising as localizing clinical signs. Pain should be increased in lesions involving the spinal nerves at or above the level of the third lumbar with flexion of the spinal column, with no increase in straight leg raising. On the other hand, lesions involving the segments of the fifth lumbar and sacral elements will result in pain early with the straight leg-raising test.

INFRAGLUTEAL RADIATION OF PAIN (SCIATICA)

There can be little doubt that damage to the structures of the low back is brought about in flexion, with or without rotary stresses, and particularly in unguarded movements or when the dorsal musculature is at a disadvantage, as in the extreme ranges of flexion. It is obvious, from the anatomical arrangement, that the structures which are liable to injury are the attachments of the muscles and ligaments, particularly the erector spinae to the ilium, and the supraspinous, the interspinous and, if a rotatory component is present, the intertransverse ligaments. Should the forces be particularly violent, the more serious lesion, namely, rupture of the disc or of the ligamentum flavum, may ensue. In this connection it is interesting to observe, as pointed out by Lewy and Groff, that there is always greater damage to the

ligamentum flavum above and below the level of the disc injury. This suggests a sparing action possibly due to the collapse of the disc and would further support the views adumbrated above.

Apart from the more major lesions involving the disc or ligamentum flavum, there is ample clinical evidence to indicate that the vast majority of cases of low back strain are due to partial or complete ruptures of the ligaments mentioned. This is indicated by the localization of the tenderness to the points of attachment of these structures, constituting, as they do, the so-called trigger points of Steindler. After such injuries the processes of repair follow ordinary physiological law. Here, however, we often deal with the chronic case where repeated small injuries with repeated efforts at repair have produced unsound healing, which in itself impedes the removal of effusion and the conclusion of the processes of repair. These lesions seem to us to be, for the most part, of the nature of chronic sprains, analogous to those which are so fully recognized in other regions of the body, as at the ankle joint. The cause of the local pain is well understood, in that both ligaments and periosteum are well supplied with sensory nerves.

The majority of the lesions of the low back occur in areas which receive their innervation from the fourth and fifth lumbar nerves. How or by what mechanism then is the radiation of pain to the infragluteal region produced? Our knowledge of this process is extremely obscure. It is generally assumed that it is a reflex process *via* the sciatic nerve. Here we meet with a fundamental difficulty. The radiation of the pain is usually to the gluteal region and posterior aspect of the thigh, but the skin of this region is supplied through the small sciatic nerve (posterior cutaneous nerve of thigh) through the first, second, and third sacral nerves, the distribution of the fourth and fifth lumbar being the skin of the leg. This radiation of pain begins in the gluteal region supplied by the third sacral nerve, and then spreads distally, passes successively to the areas supplied by the second and first sacral, in that order. If the radiation of pain was produced in this manner, it would certainly be a remarkable phenomenon, the reflex jumping from the fourth and fifth lumbar segments to the third sacral and then working backward. Owing to these facts, we feel that such a conception can be discarded.

There are certain features that characterize the radiation of the infragluteal pain. First, it is appreciated only as a subjective phenomenon. Second, there is no hypesthesia or hyperesthesia of the skin of the gluteal region or thigh. When hypesthesia or hyperesthesia does occur, as in the more serious lesions, it is found only in the skin of the lower leg properly supplied by the lumbar segments. Third, the crural pain is of a peculiar and characteristic type, giving rise to a deep burning or aching sensation. This should be contrasted with the sharp, lancinating pain experienced when extension occurs to the leg. Fourth, the pain in the thigh is distributed chiefly in the region of the ischial tuberosity, the greater trochanter, and back of the femur. Fifth, tenderness and soreness can sometimes be elicited by squeezing the musculature of the posterior aspect of the thigh. Finally, the muscle spasm, commonly associated, affects usually the erector spinae, the gluteals, and the hamstring group, all of which receive their nerve supply predominantly from the fourth and fifth lumbar nerves.

These facts lead us to propose that the radiation of pain is brought about reflexly through the nerve segments directly involved at the site of the initial lesion. The radiation of the pain follows exactly along the segmental distribution of the lower lumbar nerves to the periosteum of the skeletal structures and the attachments of the muscles.

In contrast to segmental skin innervation, known as the dermatomes, we have designated these segmental areas of skeletal innervation, following Déjerine, as the sclerotomes. Attention should be drawn to the fact that the areas of sclerotomal innervation do not agree in spatial rela-

tionship with the corresponding dermatomes.

We have ample experimental and clinical evidence to show that radiation of pain from deeper structures, such as ligaments and tendons, follows the sclerotomal rather than the dermatomal distribution. For example, the radiation of pain in subdeltoid bursitis occurs over the scapula and passes downward over the posterior aspect of the humerus, all areas supplied by the sixth cervical sclerotome. Experimental stimulation of the periosteum of the scapula with a needle produces a like radiation of pain to the elbow. A similar sclerotomal radiation occurs in "tennis elbow," in the stenosing tenovaginitis of de Quervain, and with the injection of weak solutions of formic acid. None of these radiations of pain can be explained by reference to the dermatomal or peripheral skin distribution.

We feel that the concept herein proposed, when coupled with a knowledge of the sclerotomal distribution of the nerves, will clear up several of the puzzling features with regard to the infragluteal radiation of pain and will provide a rational explanation of its mechanism as well as offering the possibility of more accurate diagnosis of the site of the initial lesion. An appreciation of the mechanism of the radiation explains the therapeutic value sometimes derived from the local injection of novocaine at the trigger point, which, by breaking the reflex arc, alleviates the pain. In long-standing cases of low back pain it is known that the chronic muscle spasm is attended by shortening of the fascial structures. Relief has been obtained by such empiric procedures as the fasciotomy of Ober and the Heyman stripping. It is clear that the benefit derived from such operations is due in part to the release of tension on the hyperesthetic periosteum.

From the roentgenologic standpoint we feel that roentgenograms of greater technical delicacy to reveal the various spinal processes, which are so often "burnt out," together with closer observation of the points of attachment of the muscles and ligaments to the skeleton, will provide inestimable diagnostic aid in the solution of these cases.

We are greatly indebted to the radiologist for his excellent work in the solution of lesions affecting the intervertebral disc and ligamentum flavum. Indeed, in the final decision as to whether or not a laminectomy is indicated, we rely primarily on his judgment. It is disappointing, however, in spite of initial brilliant postoperative results, to find a certain proportion of cases presenting a residual of painful symptoms. It is now realized that selected cases exhibiting no motor involvement, but in which a disc protrusion or herniation is demonstrable, will improve almost completely with a purely conservative regimen. We attempt to relate these variable responses to therapy, to the degree of severity of the lesion. The process is envisaged as being essentially the outcome of pressure on the spinal nerve root, and the persistence of symptoms after decompression is perhaps explained in some obscure way, as being due to the continuance of a congestive radiculitis, or perhaps to incomplete removal of the offending disc. Here again we encounter a fundamental difficulty which presents several puzzling features.

The effects of pressure on peripheral nerves have been thoroughly investigated by experimental means. A correlation has been established between fiber size and its action potential wave, on the one hand, and the function and course or distribution of the fibers on the other. It has been shown that the fibers are affected by pressure in order of their size. This means that in response to pressure, both as a stimulus and with the development of physiological block, the motor fibers are involved first, followed by proprioceptive, pressure and touch, and finally those of pain and temperature. Clinical confirmation of the experimental findings is substantial, as, for example, in the development of a crutch palsy or in cast pressure on the common peroneal nerve. Here the motor paralysis occurs early and anesthesia late. Pain is usually absent.

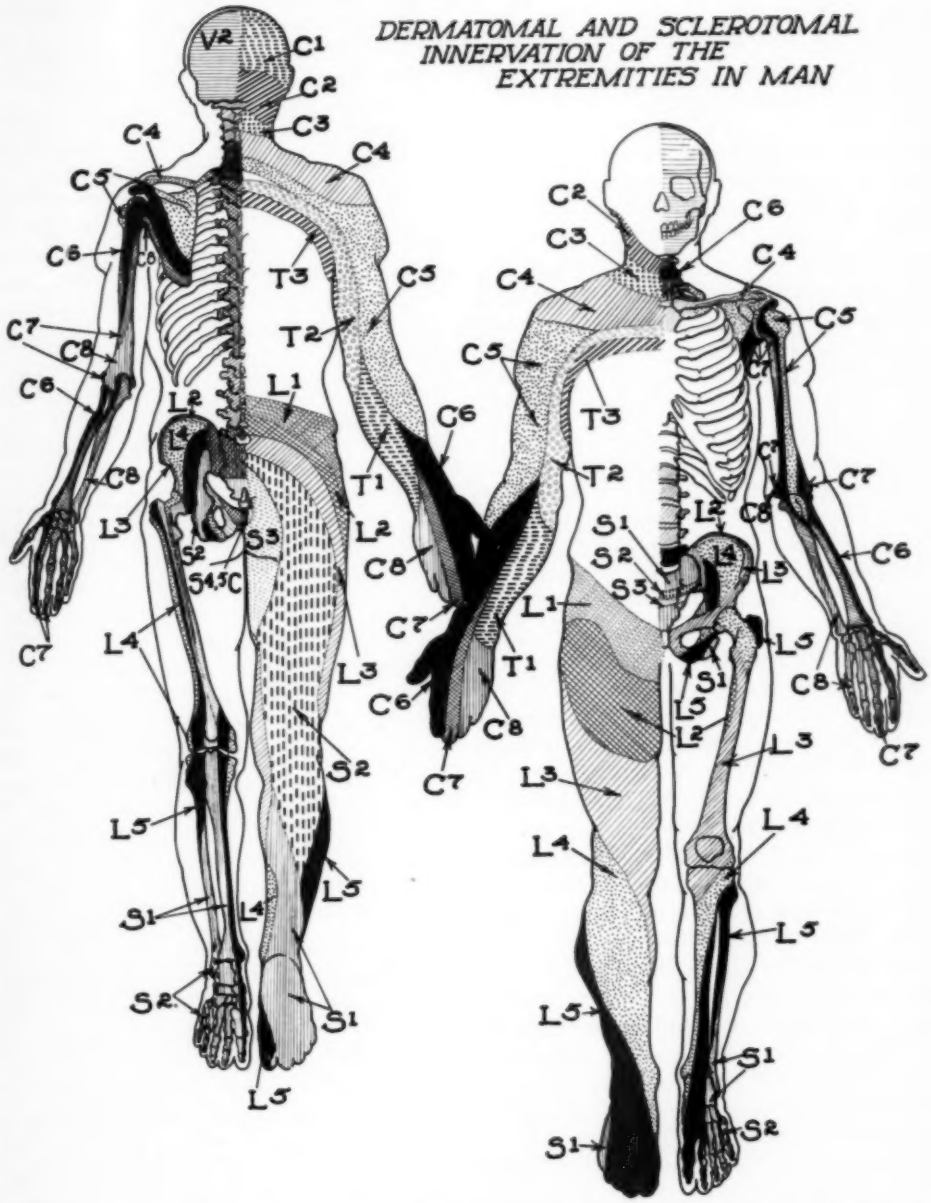

Fig. 1. Left sides of figures: Sclerotomal innervation, after Déjerine. Right sides of figures: Dermatomal innervation of extremities, modified after Foerster. Dermatome C7 has been represented, though there is some question whether the seventh cervical root has any cutaneous representation.

In posterior herniation of the disc or in ligamentum flavum injuries there is a considerable lack of harmony between the order of symptoms and what we know concerning the effects of pressure on a peripheral nerve. In these lesions pain is an early, initial, and persistent symptom, followed by the later development of muscle weakness, which may occasionally progress to a true paralysis. Last of all, hypesthesia appears in the skin of the leg and very rarely may advance to an anesthesia. After operative decompression of the nerve, the muscle weakness and hypesthesia usually disappear, but in a high percentage of cases pain persists, with radiation to the thigh.

We believe that two factors play a rôle in the symptom complex of dorsal herniation. The first is the result of pressure, mechanical or congestive, of the herniation on the spinal root, resulting in a physiological nerve block of varying degree and producing the muscle weakness or palsy and the sensory changes of the leg. These symptoms are relieved by removal of the source of pressure. The second factor is the outcome of damage to the related ligamentous structures and the establishment of a focus of irritation in relationship to the dural cuff of the nerve. It should not be forgotten that the dura is sensitive, being supplied by the recurrent meningeal branch of the spinal nerve, and histological investigation has established the existence of nerve fibers in the annulus lamellosus of the intervertebral disc. Reflex pain from this source is in our view responsible for the persistence, after operation, of symptoms in the infragluteal region, which radiation is for the most part limited to the sclerotomal distribution of the segment involved.

The dual mechanism in the genesis of these lesions emphasizes the importance of the institution of orthopedic measures as a necessary sequel to laminectomy in disc herniations if we are to improve our results. How common is the persistence of the so-called sciatica after operative removal of a herniated disc can be gathered by examination of the records of the Industrial Commission, in which the last 40 cases were given a rating of 25 to 100 per cent permanent disability. The radiologist should not fix his entire attention upon the contents of the spinal canal but should diligently search for other evidence of associated skeletal involvement.

University of California Medical School
3d and Parnassus Aves., San Francisco, Calif.

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Thorotrast and the Diagnosis of Lesions Involving the Lower Spinal Canal[1]

B. H. NICHOLS, M.D.

Cleveland Clinic, Cleveland, Ohio

THE PROBLEM presented by patients with persistent lumbago, sciatica, and sacro-iliac strain is a challenge to the acumen of most diagnosticians. Particularly does this apply to those patients who give a history of recurrent attacks over a long period of time, with no permanent relief in spite of running the gantlet of therapeutic measures reputed to cure such affections, as braces, rest in bed, physiotherapy, sacro-iliac fusion, osteopathic treatments, chiropractic adjustment, deep injection of such drugs as chloroform, and many other bizarre measures, not excluding Haarlem oil. These patients present themselves in a condition of despondency, feeling that no permanent relief is possible. In such cases our attention should immediately turn to the possibility of a protrusion or herniation of an intervertebral disc in the lower lumbar spine.

Posterior protrusion of an intervertebral disc may produce symptoms of cord compression or may simulate a tumor if the mass is large. Smaller lesions will usually compress one of the nerves as it leaves the dural envelope, resulting in unilateral pain. Most of these lesions occur between the fourth and fifth lumbar vertebrae or at the lumbosacral joint.

Most patients have a rather characteristic chain of symptoms: pain in the lumbosacral region with radiation into the buttock or the right or left hip, down the thigh into the calf, or along the lateral aspect of the leg and foot on one side. If the duration of such symptoms has been short, the case should be considered as one of recent herniation, particularly if there is a history of recent trauma. In some cases there is no sudden onset of pain, and the history is one of repeated attacks of sciatica or lumbago with prolonged periods of remission. Many patients obtain relief from the attacks by heat, rest, and physiotherapy, sometimes without subsequent recurrence. Usually, however, the attacks return, and the patient presents himself seeking a permanent cure.

Physical examination will show a list away from the side of pain. There will be hypesthesia over the side involved, particularly in the lower leg and foot, and often a diminished or absent tendon Achilles reflex on the painful side. Usually there is some atrophy of the leg in cases which have persisted over a considerable period with repeated attacks. Such findings should place a herniated nucleus pulposus among the suspected diseases.

The usual roentgen examination of the lumbosacral spine will seldom establish the diagnosis, but it may reveal the presence of other lesions, as disease of the bone, spondylolisthesis, sacro-iliac arthritis, or some abnormal anomalous condition of the spine, which will have to be eliminated as a causative factor, as any of the symptoms, physical findings, or orthopedic signs of a herniated nucleus pulposus may be present in other conditions about the lower lumbar spine. It is well to bear in mind, however, that any of these may be accompanied by a herniated nucleus pulposus, which will have to be ruled out, particularly if the symptoms persist after corrective measures have failed to relieve the symptoms. To accomplish this, some form of contrast media must be used and a spinogram made.

The subject of the most suitable contrast medium for the diagnosis of protrusion or herniation of the intervetebral disc has received much attention in the litera-

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ture during the past few years. It is interesting to note that the use of thorotrast as a satisfactory contrast medium was introduced by Tommaso Lucherini of Rome (1). In his paper, published in August 1934, he described the technic under the name "radiomyelography."

The introduction of 10 c.c. of thorotrast by the lumbar route gave a characteristic image. By this method, Lucherini made a precise study of the topography of the spinal canal with detailed relief of the intermedullary arachnoid formations. He considered thorotrast superior to lipiodol, which had been introduced by Secar, as the latter medium was easily deformed by various positions of the patient, giving at times a false impression of block; moreover, it would not infiltrate between the points of exit of the spinal nerves, and accordingly did not succeed in giving the anatomical image of a medullary sector in its more particular and finer details. Lucherini concluded that thorotrast, being a colloidal liquid, is more miscible than the iodized oils and more satisfactory for identification of the nerve root. He stated that the introduction of thorotrast was still not generally accepted, but was of particular interest to everyone. He called attention to some meningeal reaction with elevation of temperature, pain, and paresthesia after the introduction of the medium into the spinal canal. He further demonstrated that thorotrast was absorbed by the lymphatic perineural spaces, permitting visualization of the liver and spleen after spinal injection, which indicated that the elimination of spinal fluid is in part accomplished through the lymphatic perineural spaces.

Lucherini stated: "I do not believe it unwise to suggest that anybody using thorotrast should make lumbar evacuation puncture as soon as the study of the radiographic image is made, so as to extract as much as possible, removing an adequate amount of spinal fluid which has been saturated with thorotrast." He also asked: Does the thorotrast limit itself to impregnating the spinal fluid, or is it taken up by the reticulohistiocytic cells of the subarachnoid space of the endoneural membrane of the nerve fiber?

The work of Lucherini is most interesting, as it followed closely upon that of Radovici and Meller (2) of France, who injected thorotrast by suboccipital puncture and concluded that the reaction was too great. They made no further study, but advised a thorotrast solution that was isotonic with the spinal fluid and therefore non-irritating.

Capua (3), following the experience of these investigators, introduced 20 c.c. of thorotrast by the lumbar route in a patient with cancer of the head of the pancreas. He succeeded, however, in getting only a neatly detailed picture of the elements of the medullary canal; no thorotrast appeared in the spleen. Löhr and Jacobi (4) of Germany introduced thorotrast into the spinal canal with visualization of the medium a short distance along the nerve roots. This work, however, was discontinued because of the occurrence of serious reactions.

In 1938, Nosik and Mortensen (5) became interested in this subject and perfected the technic of making spinograms with thorium dioxide, subsequently removing the major portion of the medium by forced spinal drainage after the method of Kubie and Retan (6). They showed by analysis that not more than 10 or 15 per cent of the thorotrast is left in the spinal canal, an amount which has been accepted by the Council on Pharmacy and Chemistry of the American Medical Association (7) as being of not sufficient radioactivity to produce deleterious effects and too feeble to be of physiological significance.

Proceeding from this premise, we have examined with thorotrast more than 200 patients suffering with symptoms which we considered fairly characteristic of herniation of an intervertebral disc.

With the co-operation of the Orthopedic Department and the Neurosurgical Department, we have found this method most satisfactory for the diagnosis of lesions in the lumbosacral canal. In our experience

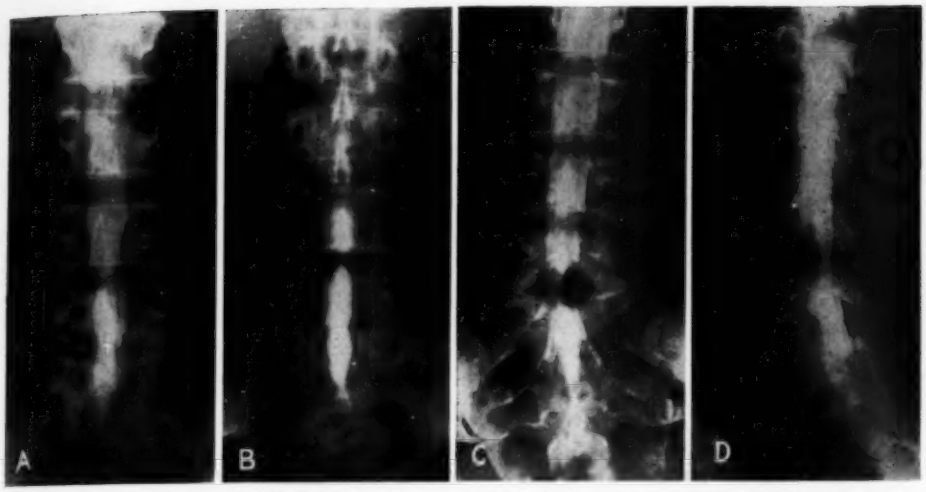

Fig. 1. A. Normal spinogram. B. Herniated disc, L4-L5. C. Large herniated disc, L5-S1. D. Large herniated disc, L4-L5.

it has proved quite accurate for the diagnosis and exact localization of a protruding disc. This accuracy is demanded by the surgical division in order that the minimal operative procedure may accomplish the desired result in each case. The side involved may readily be determined by the clinical symptoms in most instances; there is considerable variance, however, between the exact level of the lesion as determined by the clinical symptoms and the actual location demonstrable by a spinogram made after the introduction of thorotrast. The surgical findings in these lesions give us a record of the exact location of the lesion and establish the accuracy of our observations. In no instance have there been any alarming symptoms or delayed after-effects which would contraindicate a repetition of the examination. We do not approve of surgery in these cases without preliminary determination of the size, extent, and location of the condition. Two cases in which the spinogram showed no evidence of a disc herniation were operated upon on the basis of the clinical symptoms alone, and no protrusion of a disc was found. This is a small percentage, however, and a large majority of cases show the presence of the lesion at the point previously determined by clinical and physical findings (Fig. 1).

The desire to improve our percentage of correct diagnoses and proyer localizations of these lesions adds to our enthusiasm for this method of examination. This applies particularly to the smaller lesions, which we have failed to demonstrate in spinograms made by the introduction of air or lipiodol. Large lesions may be readily located by the use of any contrast medium and in most instances will present a group of characteristic symptoms which will indicate their presence and location.

TECHNIC

The patient is prepared for surgical intervention and is given a sedative one hour before the spinogram is to be made. He is brought to the x-ray department in a wheel chair. The examination is done on a combination tilt table for fluoroscopy and radiography. The patient is placed on the table, the head of which is elevated 12 or 15 degrees above the horizontal plane. In this position, lumbar puncture is done at the first and second, or the second and third lumbar space. Fluid may be taken for analysis and 10 c.c. of thorotrast injected. The patient is then observed fluoroscopically to determine the position

Fig. 2. Case 1: Normal spinogram.

Fig. 3. Case 2: Spinal block, L2-L3, due to melanoma.

of the thorotrast. Change in tilting of the table insures visualization of the lower lumbar spine. Other large lesions are readily observed fluoroscopically.

Anteroposterior and postero-anterior films are then made. Following this, the patient is rotated into an oblique position, and right and left oblique exposures are made; finally a direct lateral view is taken. If fluoroscopically there is any apparent difficulty in visualization of the lower canal, particularly in the presence of marked lordosis, films can readily be made in the upright position.

The patient is now replaced in the wheel chair and returned to bed, the head of which is elevated to a 25-degree angle. With the patient lying on the unaffected side, a large needle is inserted low in the lumbar region (if there is a large obstructing lesion, the needle is inserted above the lesion), and the draining fluid is collected. The introduction of intravenous saline solution, 45 per cent, is started, 750 c.c. being given in a one-hour period. Following this, drainage may be continued for ten to fifteen minutes, after which the needle is withdrawn. The patient is then ready for operation. If no lesion is present, he remains in bed with the head elevated for twenty-four hours.

With this method we have found it possible to recover 80 to 85 per cent of the thorotrast which has been injected. We feel that this is well within the margin of safety and have at the present time no idea of making any changes in the procedure for the thorotrast spinogram.

CASE REPORTS

CASE 1 (Feb. 14, 1938): A man, aged 35, complained of low back pain. In August 1936 he had slipped down the basement stairs and had fractured his sacrum while carrying 100 lb. of ice. Since that time he had experienced pain in the low back and

Fig. 4. Case 3: Herniated disc, L5-S1, left.

Fig. 5. Case 4: Normal spinogram.

coccyx, although he had been treated with a brace and had been in bed for six months. When seen by us he had low back pain, radiating into the posterior hip region and down the posterior aspect of the thigh to the knee. He experienced pain on lifting. Clinical diagnosis: sacro-iliac strain.

Neurological examination, July 23, 1940, showed numbness over the dorsum of the right foot.

On July 25, 1940, a spinogram (Fig. 2) was made. No protruding disc was revealed. Tentative diagnosis: coccygodynia, sacro-iliac strain. Bony fusion was advised.

CASE 2 (Aug. 12, 1941): A man, aged 43, began to have pain down the left leg in 1939. There was no history of injury. The pain was constant and of increasing severity. In February 1941 a deep muscle injection was given, which relieved the pain, but the leg became weak and the patient noticed that it was getting smaller. He began to use crutches, but his pain recurred and gradually became worse.

Examination revealed numbness down the side of the leg and absence of the patellar reflex on the left. Both Achilles reflexes were absent. Clinical impression: herniated nucleus or a spinal tumor.

A spinogram was advised, as this was considered a typical disc history, and a complete block of the canal at L2 and L3 (Fig. 3) was revealed. The tumor extended into the canal from along the course of the right 3d lumbar nerve. The nerve was involved in the tumor and was sacrificed at operation. The pathological report was melanoma.

CASE 3 (Feb. 21, 1941): A man, aged 30, complained of low back pain and pain in the left hip and down the left leg. Ten years previously, while playing baseball, he had collided with another player and injured his left hip. He recovered from this injury, but three years later the pain returned and he noticed that his leg was getting smaller. Treatment was administered for two years before the pain subsided. Seven months before admission the pain had returned after a strain to the hip, and the patient had since been under treatment.

Physical examination revealed a tender spot between L5 and S1, wasting of the left gluteal muscle, and atrophy of the calf and thigh. There were no sensory disturbances.

A spinogram (Feb. 24, 1941) showed protrusion of disc, L5-S1, left side (Fig. 4). Operative removal was successful, and the patient was well Sept. 5, 1941.

CASE 4 (Dec. 7, 1938): A woman, aged 46, complained of low back pain radiating down the back

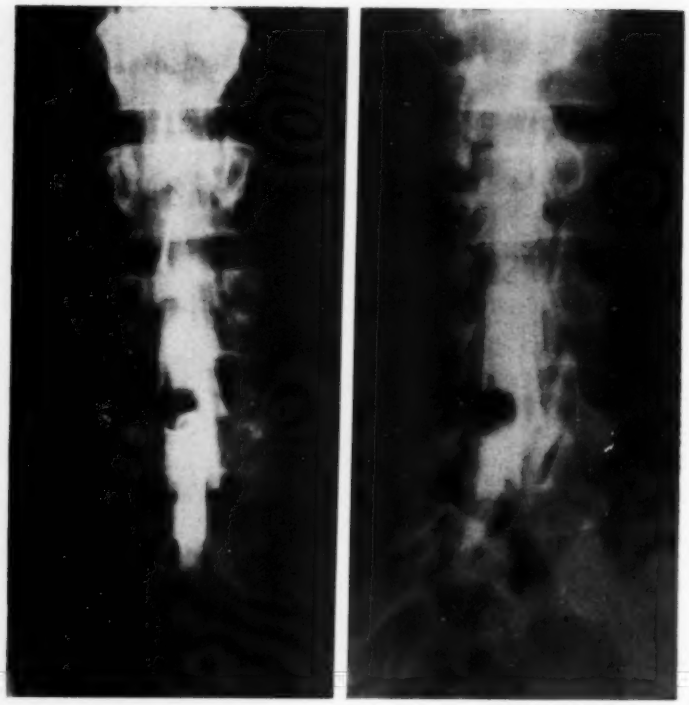

Fig. 6. Case 5: Neurofibroma, L4-L5.

of the right leg to the foot. The pain had started after a fall and had lasted for seven months. Being on her feet or lifting aggravated the pain. It was not relieved by a brace or by bed rest. The patient stood with a list; atrophy of the calf and thigh of the right leg were present. Clinical diagnosis: protruding herniated disc.

A spinogram revealed no herniated nucleus pulposus (Fig. 5), and operation (Dec. 16) showed a thickened ligamentum flavum which was removed. There was no disc protrusion.

The pain continued postoperatively, and a second operation was done April 15, 1939: epidural injection for intractable pain, sciatic. After this the patient remained in bed for several months with low back pain and sciatica, when herpes zoster developed, which increased the severity of the pain. As the disease subsided, all pain disappeared and the patient has remained well since.

CASE 5 (Sept. 20, 1940): A man, aged 24, complained of pain of increasing severity in the low back and right hip, of five months' duration. He recently had been obliged to quit work. The pain radiated to the thigh, ankle, and heel. Osteopathic treatment gave no relief. Possible disc protrusion was suspected.

Neurological examination: suspected protruding disc; no sensory changes; knee-jerk and tendon Achilles reflexes normal; no motor disorders; no loss of sphincter control.

A spinogram showed a tumor of the spinal cord at L4-L5, right side (Fig. 6).

At operation a neurofibroma, attached to the nerve root, was removed from the fourth lumbar nerve, right side.

Cleveland Clinic
Cleveland, Ohio

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DISCUSSION OF PAPERS BY INMAN AND SAUNDERS AND NICHOLS

Lyell Cary Kinney, M.D. (San Diego, Calif.): Doctors Inman and Saunders have presented an important contribution to the problem of low back pain. The demonstration of recurrent sensory nerves re-entering the interpeduncular foramen makes it clear why injury or pathology at higher levels may cause referred pain in the lumbosacral region. The analysis of pain resulting from a ruptured intervertebral disc explains well why surgery of the disc relieves the sciatica yet may leave disabling pain in the lumbosacral and gluteal regions. The essayists have emphasized the fact that a ruptured disc is necessarily accompanied by a similar injury to the adjacent interspinous ligaments. This injury of the ligaments around the interpeduncular foramen is not modified by removal of the disc fragments and still leaves an important orthopedic problem following the surgery.

This study of the nerve supply in relation to persistent and radiating pain is most timely in view of the high percentage of disability following excision of the ruptured disc. The statistics of the Massachusetts Hospital show that 25 per cent of the patients operated upon have continued compensable disability, while the State Compensation Insurance Fund of California reports compensable disability in 100 per cent of patients operated upon for disc injuries.

Doctor Nichols' paper on thorotrast brings us a beautiful and complete visualization of the entire caudal sac and neural sheaths. Such a satisfactory demonstration of detail is not possible with air or any other opaque medium available at this time. With spinal drainage after the method of Kubie and Retan to remove the thorotrast, the procedure has proved entirely safe for Doctor Nichols and his associates. By the occasional surgeon, however, the use of thorotrast must not be undertaken casually. The early German and Italian studies with this medium had to be abandoned because of the arachnoiditis resulting from the retained radioactive salt. We have all seen extrathecal injection of lipiodol; Doctor Harmby, of the University of Rochester, reports that 5 per cent of his cases showed lipiodol outside the caudal sac. Certainly this will happen occasionally, and has happened, with thorotrast, with results similar to those reported in the early experimental work.

Doctor Nichols and Doctor Nosik have done splendid pioneer work in a relatively safe method for using thorotrast. If one intends to use thorotrast for myelography, Doctor Nichols' entire technic should be followed in exact detail and with scrupulous care, both as concerns the spinal injection and the after-care of the patient.

Roentgen Therapy of Cancer of the Breast and Regional Metastases: Preoperative and Non-Operated Cases[1]

MAURICE LENZ, M.D.

New York, N. Y.

MICROSCOPIC study of mastectomy specimens from cases of cancer of the breast exposed to 200 kv. x-rays, in maximal doses tolerated by adjacent normal tissues, usually shows severe damage of cancer cells but, in our experience, not their complete destruction. In inoperable cancers of the breast this treatment ordinarily results in healing of ulceration, shrinkage of the primary and metastatic tumors, and temporary restraint of growth, but only exceptionally in five-year freedom from clinical evidence of cancer. Radical mastectomy has therefore remained the treatment of choice for patients with cancer limited to the breast, and for those in whom the primary tumor and its axillary metastases can be completely resected. Complete surgical removal is not the rule when axillary nodes are involved, as is shown by statistics of the "five-year cure rates" after radical mastectomy. According to these statistics, failures amount to roughly 30 per cent of the operated cases when the cancer is limited to the breast and to about 80 per cent when it has spread to the axilla. Because of the poor results in the latter group, preoperative and postoperative roentgen therapy has been added to radical mastectomy in the hope that the growth of unremoved local extensions and regional metastases may thus be restrained. The value of this added treatment has frequently been questioned and as yet is not completely settled.

CLINICAL MATERIAL

In an effort to obtain a clearer understanding of the rôle of roentgen therapy when used preoperatively or to replace mastectomy for cancer of the breast, a study was undertaken of the clinical histories of 82 patients with mammary cancer treated in the Radiotherapy Department of the Presbyterian Hospital, New York, between 1933 and 1937. Of the 82 patients, 44 were treated only by x-rays; in 37 a mastectomy was done after irradiation. Of the 38 preoperatively treated patients, 37 had a radical mastectomy and 1 a simple mastectomy with limited axillary dissection.

Microscopic Corroboration: The clinical diagnosis of cancer was corroborated microscopically in 17 of the non-operated patients and in all of the 38 preoperatively irradiated patients. Of the 27 patients without operation whose tumors were not examined microscopically, 25 died with clinical signs of cancer. In the operated patients the axillary lymph nodes were studied histologically at the time of the mastectomy, while in the non-operated cases they were not investigated microscopically.

Extent of Cancer: The non-operated cases and many of those referred for preoperative roentgen therapy were so extensive that complete surgical removal seemed uncertain or impossible.

Size of Primary Tumor: In Table I are given the sizes of the primary tumors before roentgen therapy. In view of the unfavorable influence which large size of the primary tumor has on prognosis of radical mastectomy, the fact that more than half of the tumors in this series measured 6 cm. or over in diameter is of especial interest.

Axillary Metastases: All of the non-operated and 31 of the 38 preoperatively treated patients had palpable, clinically metastatic lymph nodes on the involved

[1] Presented in part before the Radiological Society of North America at the Twenty-sixth Annual Meeting, Cleveland, Ohio, Dec. 2-6, 1940. The statistics have now been brought up to Jan. 1, 1942.

TABLE I: SIZE OF PRIMARY TUMOR IN BREAST

Size of Tumor	Non-operated Cases	Cases Preoperatively Irradiated
3 cm. or less	3	6
3.1 to 5.9 cm.	14	12
6 cm. or over	27	20
TOTAL	44	38

side. In 5 of the latter group the clinical diagnosis of axillary metastasis was proved wrong by microscopic examination. Further investigation showed that even large axillary masses did not always contain cancer, as exemplified by 2 of 13 patients with axillary masses 3 cm. in diameter and larger. On the other hand, cancer was found microscopically in 3 patients in whom axillary involvement had not been suspected clinically. Harrington (1) and others have drawn attention to the frequency of mistakes in the clinical diagnosis of axillary disease. It is self-evident that such unavoidable errors preclude very accurate evaluation of roentgen therapy of cancer of the breast unless complete microscopic investigation of the entire axillary contents is possible.

Local Extension and Distant Metastases: Of the 44 non-operated patients, 13 had skeletal, 4 pulmonary, and 1 liver metastasis. Five had extensive ulcerated lesions. Five showed subcutaneous nodules near the main tumor, and in 18 the tumors were either fixed to the deeper tissues or there was pronounced edema of the breast. The degree of involvement was less among the 38 preoperatively treated patients. Thirty-six of the 38 had a movable breast tumor. One was somewhat fixed to the sternochondral junction of the fourth rib and one was extensively ulcerated.

Microscopic Classification: Of the 82 cancers, 55 were studied microscopically by Dr. A. P. Stout, surgical pathologist of the Presbyterian Hospital. Seventeen of these could not be classified, 21 were poorly differentiated, 11 were well differentiated, and 2 cases were designated as intraductal, 2 as colloid, and 2 as inflammatory. These figures support the general impression that poor differentiation predominates in cancers of the breast.

TECHNIC OF ROENTGEN THERAPY

X-rays produced at 200 kv., at 25 ma., with 1 to 2 mm. Cu plus 1 mm. Al filtration and 50 cm. T.S.D., were used. The breast and adjacent chest wall were irradiated through a mesial, a lateral, an upper, and a lower field, which included the entire breast and adjacent intercostal areas. The size of the fields differed, depending upon the size of the breast and the size of the tumor, usually varying from 6 × 8 to 8 × 10 cm., but occasionally measuring 10 × 15 cm., especially when only two fields—a lateral and a mesial breast field—were used. The method of cross-firing and the dosage changed somewhat with the position of the main tumor. As a rule, the attempt was made to bring about 2,000 r/o (*i.e.*, r in air) to each of the four breast fields; a daily dose of 100–200 r/o to each of two fields was given, depending on the size of the portal and the reaction. After completion of the treatment to the breast, and at times concurrently with it, the axilla on the affected side was irradiated. About 2,000 r/o were administered to each of three fields—an anterior, a posterior, and a direct axillary field—with similar daily dosage as for the breast. Thus the total dosage to the breast was approximately 8,000 r/o and that to the axilla 6,000 r/o, given in six to eight weeks.

In irradiation of the breast, the x-ray beam was allowed to skim along the chest wall so as to avoid the lungs as much as possible. In practice the lungs cannot be completely avoided if one attempts to irradiate the anterior mediastinal lymph nodes or those of the internal mammary chain, as these lie close to the pleura. Nevertheless, radiation pneumonitis occurred rarely, was only temporary, and did not present a serious problem.

The anterior supraclavicular region, and at times a special anterior mediastinal field, were also irradiated and received, respectively, about 3,000 r/o and 2,500 r/o

TABLE II: RELATION BETWEEN SIZE OF TUMOR AND RESPONSE TO X-RAYS

Size of Tumor	Total Patients	Marked Reduction No. of Patients and Estimated Tumor Dose	No or Slight Reduction No. of Patients and Estimated Tumor Dose
3.0 cm. or less	9	8 (3096–8209 r)	1(5518 r)
3.1–5.9 cm.	26	19(411–8092 r)	7(1332–4076 r)
6 cm. or more	47	28(390–6615 r)	19(144–5462 r)
TOTAL	82	55	27

over 6 × 8 or 8 × 10 cm. fields, at the same daily rate and with the same technic as the other fields. In the operated cases irradiation of the supraclavicular field was usually postponed until after mastectomy.

SEQUELAE AND COMPLICATIONS

An interval of over a month usually elapsed between the last x-ray treatment and mastectomy. Mastectomy was not done until the radiation erythema had completely disappeared from the operative field. In only one case did necrosis of the flaps and even of the subjacent chondral cartilage follow mastectomy. This case, in which several months were required for healing, was operated on without waiting for complete subsidence of the radiation erythema. A delay of mastectomy for an average of three months from the first x-ray treatment must be reckoned with if one contemplates the administration of intensive preoperative roentgen therapy in the dosage recommended above. The larger doses produced complete desepidermization. Telangiectasia and deep sclerosis of the irradiated fields occurred in a few of the non-operated cases.

RESPONSE OF THE PRIMARY TUMOR TO X-RAYS

An attempt was made to study the radiosensitivity of the individual cancers by recording the gross reduction in size and the microscopic changes in the primary tumor following certain x-ray doses.

Size of Tumor and Response to Irradiation: Response to roentgen therapy seemed to be influenced by the original size of the growth. Of the 82 cases, 27 failed to regress, as seen in Table II. The marked variation in dosage is accounted for not only by considerations of the size of the tumor, but by local, general, and at times extraneous factors beyond our control.

Tumor Dose and Regression: The tumor dose was calculated on the basis of depth dosage tables at the point assumed to be the center of the tumor. The tumor was measured and the distance from the skin to the center was estimated. The size and number of fields used and their relative position in relation to the assumed center of the tumor were taken into account in estimating the depth dosage. It is realized that this approximated tumor dose is of only comparative value. In view of the variety of dosage which produced radiation changes, other factors beside the quantity of x-rays reaching the cancer must have influenced the response of the breast tumor to roentgen therapy. Some of the largest tumors were reduced in size after a tumor dose as small as 390 r, while others of medium size failed to respond to a tumor dose of 4,076 r. A definite relationship between x-ray dosage and reduction of the cancer, therefore, could not be deduced from the data at hand. Nevertheless, an impression was gained that the larger doses were on the whole more effective.

Relation between Response of Tumor and Its Microscopic Structure: The 55 (17 non-operated and 38 operated) cases in which material for microscopic study was available were classified microscopically by Dr. A. P. Stout. They were then divided into two groups, the one showing marked reduction and the other no reduction or only slight reduction. The results of this analysis are given in Table III.

Among the poorly differentiated tumors

TABLE III: GROSS RESPONSE TO X-RAYS IN 55 CANCERS CLASSIFIED MICROSCOPICALLY

Microscopic Classification	Total Cases (number)	Cases Showing Marked Reduction in Size	Cases with No or Slight Reduction in Size
Poorly differentiated	21	13	8
Well differentiated	11	9	2
Intraductal	2	2	..
Colloid	2	2	..
Inflammatory	2	..	2
Unclassified	17	13	4
TOTAL	55	39	16

there were nearly twice as many which failed to be reduced by roentgen therapy as among the well differentiated carcinomas. This corresponds to the experience of Knox (2), who states that "in general it appears that the more differentiated carcinomata of the breast are more easily influenced by radiation." Stewart (3) believes that except in intraductal carcinoma and comedo types he "cannot predict the radiation behavior of cancer of the breast with any degree of accuracy." These views are contrary to those of the majority, who believe, as emphasized by Harrington (4, 5), that roentgen therapy is useful chiefly in the undifferentiated and not in the well differentiated carcinomas of the breast. The groups in Table III are too small, and the sizes of the tumors and the x-ray doses too varied, to permit definite deductions. It cannot be claimed, therefore, that a striking difference in the response of the tumor to x-rays depending exclusively on its microscopic type has been shown. On the contrary, it is suggested that there are other factors beside the microscopic character of the cancer which are concerned in its radiosensitivity, such as extent, infiltration, accessibility, and probably x-ray dosage. It should also be noted that Table III deals exclusively with radiosensitivity of the cancer, without regard to radiocurability, whereas most reports in the literature do not differentiate between the immediate response to irradiation, *i.e.*, radiosensitivity, and the ultimate cure by irradiation, *i.e.*, radiocurability.

Microscopic Changes after Irradiation: The microscopic changes resulting from irradiation were studied in all cases in which material was available, but were best observed in 9 instances in which a biopsy specimen from the breast before roentgen therapy could be compared with the mastectomy specimen after this treatment. In general, these changes followed in degree the gross evidence of the effect of irradiation. They were slight when reduction in the size of the tumor was moderate and more pronounced when gross shrinkage was marked. As most of the mastectomies were done within two months of the last x-ray exposure, earlier radiation changes were principally observed. Thus there were noted vacuolization, pyknosis, swelling of cells and nuclei, reduction in the number of mitoses, and atypical mitoses. In a few cases sclerosis of the stroma, which was absent or slight in the biopsy specimen, was marked in the excised breast. The mastectomy specimen from one patient (P. H. No. 422,200), who was operated on thirteen months after the last x-ray exposure, showed a marked radiation sclerosis not present in the original. Most mastectomies were probably done too soon after completing roentgen therapy to allow time for radiation sclerosis. Dr. Stout's findings in these 9 cases, correlated with x-ray dosage and gross reduction of the tumor, are given in Table IV.

In spite of the large x-ray doses which had been administered, in this series of cases recognizable cancer cells were found in all mastectomy specimens. This does not correspond to the experience of others (6), who were unable to find persisting cancer in some heavily irradiated mastectomy specimens. In the examination of the mastectomy specimens in this series, Dr. Stout and his staff sometimes made as many as forty and fifty sections from a case, including those areas of the breast in which there was no gross evidence of cancer. In one instance, only 20 poorly stained cancer cells could be recognized

TABLE IV: MICROSCOPIC CHANGES AFTER IRRADIATION

Gross Reduction of Tumor		Microscopic Changes	Radiation Effect on Persisting Tumor			Estimated Tumor Dose (r)	Period of Treatment (days)	Average Number and Size of Breast Fields	Interval from Last Day of Treatment to Mastectomy (days)
			Mitoses per high-power field		Cellular degeneration				
Size before biopsy (cm.)	Size before mastectomy (cm.)		Biopsy	Mastectomy	Mastectomy				
12 × 9 × 8	4 × 3.5 × 2.5	Tumor and stroma show definite evidence of radiation effect. Gray degeneration. Much tumor remains	1 per 3	1 per 3–4	Slight (vacuoles and swelling)	2560	24	4 (10 × 10)	39
10 × 10	2 × 4	Remaining tumor well preserved, especially inside ducts. Much of tumor well differentiated. Bizarre mitoses	1 per 1	1 per 10	Slight (swelling and pyknosis)	1782	43	3 (10 × 10)	32
6 × 7 × 5	0	Only traces of tumor remain. Well differentiated intraductal carcinoma without mitoses; marked stromal effect	None seen (aspiration biopsy)	0	None (?)	3780	31	3 (8 × 10)	45
5 × 4	2.5 × 4.5	Much tumor remains in breast	Only cervical node	1 per 3	Slight (vacuoles)	411	3	3 (8 × 10)	2
4 × 3 × 3	Reduced	Tumor cells remain as isolated units in dense fibrous tissue	Only axillary node	0	None (?) (vacuoles)	3559	24	3 (10 × 15)	37
3 × 3	Much smaller	Tumor cells well preserved in considerable quantity. Mitoses hard to find	Not available	Rare	None	3096	40	2 (10 × 15)	27
2 × 2	0	Only 20 cancer cells found	1–2 per 1	0	Marked (vacuoles)	4050	27	1 (8 × 10)	394
4.5 × 4.5	4.5 × 4.5	No effect in places; marked in others	0	1 per 8	None in places; marked in places (pyknosis; vacuoles)	1890	48	1 (8 × 10)	38
4 × 3	3 × 3	Absence of mitoses is only radiation effect	1 per 10	0	None	3750	36	2 (6 × 8)	41

As seen in the above table there was in some cases little microscopic evidence of tumor damage, even though gross regression of the tumor was marked. This indicates that destruction of a great deal of tumor tissue may occur, yet the persistent remnants of the tumor which have escaped destruction often show no evidence of cellular degeneration. It is also quite possible, as brought out by Halley and Melnick, that after four to five weeks following irradiation, and with tumor doses of 1,200–4,500 r, regrowth of the surviving tumor cells may take place (15).

in the entire breast. The finding of so few recognizable cancer cells suggests a profound radiation effect and clinical growth restraint, probably for years. The viability of such poorly stained cancer cells may be questioned, yet this finding does not permit the claim of complete "sterilization" or destruction of the cancer.

The effect of roentgen therapy was less marked in the metastatic lymph nodes in the axilla. In one of the 9 cases, the axillary node obtained by biopsy before irradiation was compared with those removed at the time of mastectomy, *i.e.*, after irradiation with 2,000 r in nineteen days, directly to the axilla (200 kv., 25 ma., 2 mm. Cu plus 1 mm. Al, 50 cm. T.S.D., 8 × 10 cm.). The specimen was examined thirty-seven days after the last x-ray exposure and showed a marked variation of the x-ray effect in the various lymph nodes. In some nodes there were pronounced vacuolization of the cells and absence of mitoses, while others appeared not to have been touched by the irradiation. It was not possible accurately to correlate these changes with the x-ray dosage reaching the various nodes, and we have no adequate explanation for these differences.

From the standpoint of microscopic appearance, therefore, the x-ray doses which were given were insufficient to destroy all cancer cells in the breast and in the axillary nodes, though there was gross reduction of the tumor and microscopic evidence of severe damage to many cancer cells.

To recapitulate, one may say that the immediate reduction of the breast tumor after roentgen therapy in this series seemed to vary inversely with the size of the tumor; the microscopic character of the tumor had little bearing on its response; a relation of x-ray dosage to the response of the tumor could not be ascertained, as some medium and large tumors responded to small doses while some small tumors failed to respond to large doses. Microscopic evidence of radiation damage was more marked in the breast tumors than in the axillary lymph nodes, but recognizable cancer cells were found in all cases after irradiation.

SURVIVAL

Axillary Involvement, Operated Group: Of the 38 preoperatively irradiated patients, 22 were operated on five or more years ago. Of these, 9 are now free from clinical evidence of cancer for five years or longer after mastectomy; 2 others survived for a similar period but died of cancer later. Of the 22 patients, only 3 failed to show axillary metastases on microscopic examination at the time of mastectomy. These 3 are included among the symptom-free cases, though 2 of them had extensive breast lesions. It is questionable how much roentgen therapy contributed to the survival of these patients. Six of 18 patients with extensive cancers and axillary involvement are symptom-free for more than five years. While the group is too small to permit definite conclusions, it is suggestive that one-third of the patients are well after five years, whereas the accepted five-year clinical cure rate in this group of cases after radical mastectomy alone is only 20 per cent.

In a series of 78 cases published previously (7) moderate doses of low-voltage x-rays had been administered after radical mastectomy to the mastectomy area, the homolateral axilla, and supraclavicular region. Of this series, 12 did not have axillary involvement; in 25 involvement was limited to the lower pectoral group, and in 41 the lower and upper groups of axillary nodes were invaded. The five-year freedom from cancer in these three groups was, respectively, 58 per cent, 20 per cent, and 7 per cent, showing the tremendous influence which axillary invasion has on the results of mastectomy followed by roentgen therapy.

In the present series of preoperatively irradiated patients, a similar though much less pronounced *effect of the extent of axillary involvement on survival* is noted. As stated above, the cases were locally

TABLE V: INFLUENCE OF AXILLARY INVOLVEMENT ON RESULTS OF PREOPERATIVE ROENTGEN THERAPY

(38 patients)

Axillary Nodes	Patients Treated	Symptom-free Patients*	Patients Alive with Disease	Dead
None	11	5	0	6
Up to 2.5 cm. in diameter	14	5	0	9
Larger than 2.5 cm.	13	3	2	8

* 4 years or longer after mastectomy.

more extensive than the average early operable group; otherwise they would not have been submitted to preoperative roentgen therapy.

The four-year survivals after mastectectomy, grouped according to extent of axillary involvement, may be gleaned from Table V. The nodes were measured before irradiation and the diagnosis corroborated microscopically at the time of mastectomy.

Size of Breast Tumor and Survival: The size of the breast tumor had a prognostic significance somewhat similar to that of the axillary nodes, though not as marked. In the series of 78 postoperatively irradiated patients referred to previously, 51 patients had tumors less than 5 cm. in diameter. Of these, 23.5 per cent were free from clinical signs of cancer five years after roentgen therapy. Of 27 patients with tumors larger than 5 cm., only 11 per cent were well for a similar length of time. The preoperatively irradiated group shows the same tendency (Table VI). The figures imply that the larger tumors have a less favorable prognosis than the smaller ones.

Tables V and VI suggest that the extent of axillary metastases and the size of the tumor in the breast had a definite bearing on the survival of patients after mastectomy and preoperative roentgen therapy.

Microscopic Structure of Cancer and Survival: The influence of the microscopic structure of the cancer on survival could not be deduced from the information available. The general impression that the poorly differentiated tumors do worse than the well differentiated is probably correct, but the material in the present series of cases is insufficient to support this view effectively. Only 17 of the 44 non-operated cases were corroborated microscopically. Of the 55 cases in which microscopic classification was attempted, 17 could not be classified.

TABLE VI: SIZE OF BREAST TUMOR AND SURVIVAL

Size of Tumor	Number of Patients Treated	Free from Symptoms	Alive with Disease	Dead
Less than 3 cm.	6	4	0	2
3.1 to 5.9 cm.	12	4	0	8
6 cm. or more	20	5	2	13

Tumor Regression and Survival: Investigation of the relationship between the response of the breast tumor to roentgen therapy and the survival period of the patient yielded some interesting findings. The survival of the patients from the first roentgen treatment to Jan. 1, 1942, was studied. In the 38 patients treated by preoperative irradiation and radical mastectomy, it averaged sixty months for the 31 patients whose breast tumors showed marked regression as compared to thirty-six months in 7 similarly treated patients in whom the tumors changed little or did not regress. In half of the 44 inoperable cases, the tumor was reduced markedly after roentgen therapy. The average survival for these patients was twenty-seven months as compared to ten months in the group of patients in whom the tumor was not reduced. These findings suggest that marked reduction of the breast tumor after roentgen therapy has a favorable prognostic significance. It should be remembered in this connection that more of the smaller and well differentiated cancers regressed after this treatment and that the prognosis in these cases is likely to be better than for the larger and less differentiated tumors.

Natural Clinical Course and Survival: In addition to the factors discussed so far, survival was also influenced by the natural

clinical course and growth rate of the tumor. Attention has frequently been called to the importance of this factor in the progress of cancer of the breast, *e.g.*, by Nathanson and Welch (8), Luff (9), and others. Lee's clinical index of malignancy also emphasizes rate of growth among other considerations (10). Though patients with a rapidly growing cancer of the breast are likely to seek medical advice sooner after discovery of the tumor than those with a slowly developing growth, survival is likely to be longer in the latter type, irrespective of treatment. Patients with slowly growing tumors have a tendency to longer survival even after dissemination of the disease, as the metastases also grow more slowly. In the chronic case, the clinical appreciation of the limits of the cancer—and therefore the accuracy in outlining the necessary treatment fields—is more likely to be correct than in the acute case. In the latter, inadequate irradiation fields are frequently chosen as the diffusely growing cancer has silently spread beyond the readily recognizable borders.

While the number of patients in the present series is small, the following observations are suggestive. On admission, 27 of the 44 inoperable patients had symptoms associated with cancer of the breast for less than one year. Their average survival was sixteen months. In 15 other patients, symptoms were present one year or longer; their average survival was twenty-two months. One of the patients, with a sixteen-year history of a breast tumor, was admitted with skeletal metastases and survived three and a half years after admission. Occasionally we have seen patients with skeletal metastases secondary to slowly growing cancers of the breast who survived five or more years after these metastases were radiographically demonstrable.

Criteria of Operability: The preoperative estimate of operability in cancer of the breast is frequently too optimistic. This probably accounts for most of the failures of radical mastectomy. Unrecognized local extensions, regional metastases beyond the field of removal, and distant metastases progress after mastectomy and finally result in the death of the patient.

The criteria listed below have been suggested by Stout and Haagensen of the Presbyterian Hospital and have been of help in our experience. These workers believe that cases conforming to their classification of "inoperable" are preferably treated solely by roentgen therapy and not by a combination of roentgen therapy and surgery. They feel that once a case is inoperable, it remains inoperable even though marked improvement may take place after roentgen therapy. They have seen wide dissemination of cancer soon after mastectomy in those cases which, though originally inoperable, were apparently made operable by irradiation therapy. Their criteria of operability follow:

Radical mastectomy should be done in all women with carcinoma of the breast whose general condition permits major surgery, whatever their age, and even though the lesion be bilateral, except under the following conditions, which are indications that surgery will not cure.

(1) Development of a breast tumor during the course of pregnancy or lactation.
(2) The so-called "inflammatory" type of breast carcinoma (diffuse enlargement of the breast, redness, edema, and elevated temperature of the skin).
(3) Extensive edema over the breast (more than one-third of the skin affected).
(4) Satellite tumor nodules in or beneath the skin over the breast or adjacent chest wall.
(5) Intercostal or parasternal tumor nodules.
(6) Edema of the arm.
(7) The presence of any two or more of the following signs of locally advanced breast carcinoma (one does not suffice).
    (*a*) Ulceration of the skin.
    (*b*) Edema of the skin over the breast of limited extent (less than one-third of the skin affected).
    (*c*) Fixation of the tumor to the chest wall.
    (*d*) Fixation of the axillary lymph nodes to the skin or to the deeper structures of the axilla.
    (*e*) Axillary lymph nodes measuring 2.5 cm. or more in transverse diameter.
(8) Proved or clinically unquestionable supraclavicular metastasis.
(9) Distant metastasis to the contralateral axilla, lungs, bones, liver or elsewhere.

Statistical Comparisons: As repeatedly emphasized by Portmann (11) and others, it is desirable to group all patients with cancer of the breast treated by roentgen therapy according to the extent of involvement. Microscopic support of the clinically estimated extent of the cancer is manifestly impossible in the inoperable group, in which complete microscopic investigation is not done during life. Yet survival, as previously shown, is directly related to the extent of the cancer when treated. Only those comparisons of survival rates are valid in which the extent of the disease in the cases which are being compared is similar. Thus one cannot compare cases which have been classified only on a clinical basis with those classified microscopically.

Other Prerequisites for Comparison of Cases: The importance of comparing only series of similar anatomical extent and similar clinical character is generally accepted. Less attention is paid to the prerequisite that the technic of roentgen therapy in both series of cases also be comparable. Series of cases are compared which have been treated by all types of technic, and sometimes by radiologists from widely different parts of the country (12). Definite conclusions are nevertheless drawn as to the value of roentgen therapy. The all-inclusive terms, preoperative and postoperative roentgen therapy, are used without specifying such data as total and daily dosage, fields, filtration, etc. The importance of these details needs hardly to be emphasized. The amount and distribution of x-rays reaching the deeper tissues, for instance, are quite different if the same number of r/o are administered postoperatively to the supraclavicular, infraclavicular, axillary, and mastectomy areas on the affected side through a single large field, as is done by some radiologists, or through four individual fields.

Because of the rapid development of roentgen therapy, new methods have been tried constantly. Roentgen therapy of cancer of the breast during 1910–20 was quite different from that applied during 1930–40. Unfortunately it is difficult to find large series of mastectomies with similar clinical, anatomical, and microscopic characteristics, treated with and without preoperative or postoperative roentgen therapy, in which the x-ray technic has remained sufficiently constant, through the period under investigation, to permit of its reliable evaluation. The confusion which exists with regard to the value of preoperative and postoperative irradiation is no doubt partially due to differences in tumor doses, as cases have been compared which have been treated by totally different, non-comparable types of technic.

VALUE OF PREOPERATIVE ROENTGEN THERAPY

There is general agreement as to the palliative value of roentgen therapy in inoperable cases. There is also no doubt as to the frequent reduction in size of the breast tumor and axillary metastases by preoperative treatment as given in this series. The necessary delay of three months before mastectomy in the latter method, and the fear that metastasis may occur during this period of waiting, have caused many surgeons to hesitate to recommend preoperative roentgen irradiation in spite of the known poor results of radical mastectomy in cancer of the breast with axillary involvement. The demonstration that, following preoperative roentgen therapy, there is often regression or at times disappearance of the palpable breast tumor is worthy of note. The survival of operated and non-operated patients in whom the tumor was thus shown to be radioresponsive was longer than in those in whom the tumor did not regress. One-third of a small group of preoperatively irradiated patients with axillary involvement were clinically free from cancer five or more years, whereas one-fifth is the generally accepted figure for this group treated only by mastectomy. The longer survival of these two groups of preoperatively irradiated patients does not support the apprehension that metastasis may occur during the waiting period, and agrees with the

views of Bloodgood (13), Lee *et al.* (14), who do not share this fear. In cases which are on the borderline of operability, but have none of the definite characteristics of inoperability mentioned above, it would seem justifiable, therefore, to try preoperative roentgen therapy. If a two or three weeks' trial results in regression of the breast tumor, complete preoperative therapy as outlined above may be given; if not, immediate mastectomy should be done. No attempt is made to postulate hard and fast rules. This seems a reasonable attitude for the present, but may be changed in the future.

The reasons for irradiating the breast and axillary nodes which will later be resected, instead of limiting the preoperative roentgen therapy to surgically irremovable drainage areas, are based on the following considerations: Preoperative roentgen therapy of the breast tumor and axillary metastases may cause temporary regression of these masses. It also produces degeneration of many cancer cells and reduces the number of mitoses. If such degenerated cancer cells are dislodged during mastectomy, they are likely not to have the same growth vitality as undamaged cancer cells.

The degree of gross regression of the cancer in the breast and axilla may serve as a guide to the response which may be expected in metastases in such regions as the internal mammary chain of lymph nodes and anterior mediastinal lymph nodes, since they are inaccessible to clinical observation. It is unlikely that cancer will be destroyed completely in these lymph nodes by present-day preoperative or postoperative therapy with 200 kv. x-rays. In none of the breast or axillary nodes in this series was complete destruction of the cancer observed microscopically. The doses which reached the cancer cells in the breast and in the axilla were much larger than those which in practice may be brought to bear on cancer cells in the lymph nodes of the internal mammary and anterior mediastinal chains.

Nevertheless, growth restraint was observed clinically in many of the primary tumors and in axillary metastases. A similar effect may be expected in other irradiated metastases. If there are clinically unappreciable metastases in the nodes of the internal mammary and anterior mediastinal chains, in the intercostal or the clavicular regions, they may be assumed to be very small. Small cancer masses are likely to be more easily affected by roentgen therapy than larger masses. In spite of the fact that it is impractical to deliver as high x-ray doses to these areas as were given to the breast tumors in the present series, it is probable that sufficient may be administered to cause a certain amount of growth restraint and thus prolong life.

We prefer preoperative to postoperative roentgen therapy. In preoperative roentgen therapy one deals with a cancer which has not been disturbed, except perhaps by biopsy. Larger dosage may be administered to the chest wall than in postoperative treatment, because of better nourishment and vascularization of the tissues, which have not been interfered with by surgical trauma.

SUMMARY

A study was made of the clinical histories of 82 patients with cancer of the breast receiving roentgen therapy at the Presbyterian Hospital, New York, between 1933 and 1937. In 38 of these patients this treatment was followed by radical mastectomy. The small number of cases precludes definite conclusions, but the findings are interesting and suggestive.

For the non-operated and operated groups the survival period was longer in those patients in whom the breast tumor regressed after roentgen therapy. The proportion of five-year freedom from clinical evidence of cancer in patients with involvement of the axilla was higher than is usually reported in similar groups treated only by radical mastectomy. Survival among the non-operated patients was longer when the clinical course of the primary tumor suggested a tendency to slow growth than when this tended to be rapid. Gross and microscopic evidence of regression was more

marked when the primary tumor was small and less marked when it was large. The radiation effect was more pronounced in the breast than in the axillary lymph nodes. The degree of regression could not be correlated with the microscopic structure of the tumor or with the tumor dose.

180 Fort Washington Ave.
New York, N. Y.

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DISCUSSION

U. V. Portmann, M.D. (Cleveland, Ohio): It is very gratifying to have someone use the classification for cancers of the breast that I have been advocating for several years. It is interesting, moreover, that in using this classification in a large series Dr. Lenz and his associates have found the relative proportion of cases and the results of treatment in each of the three groups in close conformity to statistics which I have published.

I recently revised the classification which Dr. Lenz has used, since a certain percentage of patients have distant metastases when first examined. These should be placed in a different category from others in analyzing the results of different methods of treatment, especially because surgeons do not wittingly operate upon them. I have therefore added a fourth group in this newer classification, although the three other groups are based upon the same criteria as formerly. My fourth group comprises cases having extensive axillary or supraclavicular lymph node involvement or evidences of distant metastases clinically demonstrable.

In his discussion Dr. Lenz has talked principally about Group III cases, that is, those cases having clinical manifestations of surgical incurability. I have not yet studied our series of cases to determine the proportion of Group III cases having distant metastases when first examined and therefore classifiable in Group IV. Dr. Lenz, however, has found that 16 of 44 cases, or 40 per cent of his Group III patients, had distant metastases. This suggests that about 40 per cent from Group III should be placed in a different category (Group IV) because the extent of disease precludes the possibility of cure, and operations under these conditions are not, or should not be, performed.

I believe Dr. Lenz has been too apologetic for the lack of biopsies in 27 of his Group III cases. Perhaps we radiologists are being bluffed into the necessity for biopsies to prove that the patients we treat really have cancer of the breast. The cases he has talked about showed frank clinical evidences of cancer, and the chance of error in diagnosis is very remote. Patients have been operated upon for cancer of the breast with no better evidences of the character of the lesion. Radiologists should have the same consideration in regard to the accuracy of diagnosis based upon clinical manifestations.

Dr. Lenz has found, and I agree, that the size of a tumor is no indication of what its response to irradiation may be. Small, slowly growing cancers that are well differentiated and radioresistant respond quite differently from others that may be large, vascular, and often more radiosensitive.

It was emphasized, also, that histologic grading of cancers of the breast is of only incidental interest, but of no significance in regard to the possibility of sterilizing the breast of cancer by irradiation. We seldom are able to sterilize the breast and probably never destroy all cancer cells in the axillary lymph nodes. This is one reason why I believe that Group III cases should not be operated upon after irradiation, because not all of the cancer can be eradicated either by this treatment or by the most

radical surgical procedure. The patients therefore will not be cured. Why not devote our entire attention to irradiation and do nothing else?

It is shown that approximately 50 per cent of Group II patients treated only by operation survive five years, or may be considered cured. These have only a few axillary nodes involved and no clinical evidences of incurability which would put them in Group III. However, 50 per cent of Group II cases are not cured by operation alone and, therefore, cancer must have remained. I am sure that pathologists cannot always determine whether or not all the cancer has been removed at operation in this particular type of case. All such patients should therefore have irradiation postoperatively to delay growth, thereby prolonging life and economic usefulness.

Dr. Lenz has advocated preoperative irradiation for certain cases which he calls "borderline" between Groups II and III. There are several reasons why I think it would be difficult to make the selection on the basis of clinical findings.

First, the selection could not be based logically upon examination of the axilla, because the presence of metastases in this location cannot be detected by palpation in more than half of the cases in which the lymph nodes are actually involved, and approximately 25 per cent of all cases have no metastases. Therefore, in the absence of clinical manifestations of advanced disease or incurability as regards the breast, it is impossible to tell in a great many instances whether a case should be considered as belonging to Group I, without axillary metastases, or Group II, in which only a few lymph nodes are involved. The difference can be ascertained only after operation and examination of the axillary tissues removed. I doubt that Dr. Lenz would advocate preoperative irradiation for patients without palpably enlarged axillary lymph nodes or clinical evidences of advanced or incurable cancer in the breast.

Second, there are some patients who have no clinical manifestations of advanced incurable cancer in the breast, but do have extensive axillary metastases in numerous nodes too small to be palpable. On the basis of clinical examination, such cases might be considered Group II but not Group III cases. Preoperative irradiation would not be suggested for such cases according to the criteria Dr. Lenz has mentioned because the actual extent of disease which would make them Group III cases as far as prognosis is concerned cannot be ascertained until after microscopic examination o all lymph nodes removed.

Third, a large proportion of patients with palpably enlarged axillary lymph nodes also have evidences in the breast of advanced and incurable cancer, which makes them frank Group III cases. Preoperative irradiation will not eradicate all of the cancer from the breast or axillary nodes; therefore, the disease is still as extensive after irradiation as before, and it still cannot all be removed surgically, nor can the patient be cured. I feel quite sure that Dr. Lenz agrees with me that a patient with clinical manifestations of advanced or incurable cancer of the breast cannot be made curable by irradiation. I cannot understand, therefore, how patients with cancer of the breast are to be selected for preoperative irradiation on the basis of the clinical manifestations of the extent of disease.

Dr. Lenz has come to other conclusions with which I heartily agree: first, that we should classify cases of cancer of the breast according to the extent of disease when making comparisons of different methods of treatment; second, that patients with clinical evidences of advanced cancer of the breast or Group III cases should be treated by irradiation alone to delay the growth and thereby prolong life and economic usefulness for some of them.

Edward Holman Skinner, M.D. (Kansas City, Mo.): The essayist has shown and the preceding pathologist has exhibited the fact that we have not been able to deliver a useful and bearable lethal dose of irradiation to carcinoma of the breast under any circumstances. An ambitiously large dose or even theoretically complete dose may bring both disaster and unhappiness to the patient. But patients have been clinically improved by moderate dosage. I am therefore impressed with the advantages of conserving our patients, both economically and physiologically, by reducing the size of the ports to the areas of involvement. With small ports it is possible to give larger dosage without sacrificing skin integrity. Large areas require protracted series of treatment, with longer hospitalization and many upsets in family economy. Very large x-ray doses may be given at weekly intervals if small skin areas are used. We feel that with this method the ultimate statistical results will be comparable.

Possibly by now we have proved to ourselves what the surgeon has known a long time, *i.e.*, that we are not curing these cases and that we cannot deliver a full theoretically lethal dose without disaster. We had better be content with what may be termed a physiological or biological x-ray dosage.

Characteristic Bone and Joint Changes in Compressed-Air Workers: A Survey of Symptomless Cases[1]

A. L. L. BELL, M.D., F.A.C.R.
Professor of Radiology, Long Island College of Medicine

GEORGE N. EDSON, M.D., L.L.M.
New York State Department of Labor

NEWTON HORNICK, M.D.
Long Island College of Medicine

BONE CHANGES in compressed-air workers were first described by Bornstein and Plate (3) and, independently, by Bassoe (1) in 1911. In 1939 Kahlstrom, Burton, and Phemister (15) reported four cases of multiple bone lesions in caisson workers. One of these patients was examined at autopsy, and the bone pathology was described. These same authors (16) later presented additional cases of aseptic bone infarction with similar lesions, of undetermined etiology, in patients who had never worked in compressed air. Between 1911 and the present time the condition has been described by several other writers, notably Coley and Moore (8), Walker (27), and Rendich (22).

Bone changes of the type described by Bornstein and Plate (2, 3), and by Kahlstrom, Burton, and Phemister (15, 16), were seen on films presented to the Labor Department of the State of New York in compensation cases where the lesions were supposed to have been caused by a single injury. The shaft and epiphyseal findings, as noted by Dr. Edson of that Department, were the typical ones described by the earlier writers, and all of the men in whom these changes were seen were at the time, or had previously been, caisson workers. In all, 30 such cases were observed in a two-year period (1939–41). Since the injuries sustained quite obviously did not produce the changes, and since other bones not in the area traumatized showed similar pathology but no symptomatology, it was felt that an x-ray study of the long bones of a group of caisson workers presenting no clinical symptoms would be of interest, particularly since bone changes had always been considered a rare occurrence in these workers.

There is historical mention as far back as 460 B.C. of sponge and pearl divers working at depths which would subject them to rapid changes of pressure. No resulting symptoms are mentioned, presumably because of the short duration of the exposures to increased pressure. Compressed air was introduced into industry in 1678 by John Smeaton, who successfully operated a diving bell necessitating its use. Before this, in 1664, Dr. H. Henshaw had suggested the use of compressed air in the treatment of disease, but this method was not tried until after Junod published a report on the subject in 1836. Hamel, in 1820, and Colladen, in 1826, observed symptoms of neuralgia following exposure to compressed air. As far as is known, these were the first descriptions of such symptoms. Compressed air was used in a mining project by the French engineer, Triger, in 1841, and symptoms following exposure of the workers to the increased air pressure were described. In 1845 two French physicians, Pol and Watelle, published the first paper of scientific value on this subject.

THEORIES AND PATHOGENESIS

During the past fifty years many workers have been subjected to increased pressure while engaged in caisson work connected with the drilling of water mains and the construction of tunnels under bodies of water. Since the first half of the nineteenth century there have been many at-

[1] Under the auspices of the New York State Department of Labor, Honorable Frieda S. Miller, Industrial Commissioner.

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tempts to propound a theory which would explain the symptoms following rapid transition from a high to a lower atmospheric pressure. These theories may be grouped by cause as follows: first, exhaustion and cold; second, mechanical congestion; third, the recent theory of gas embolism.

There have been numerous proponents of the first theory, namely, that attributing the symptoms to exhaustion and cold—Bouhy, in 1848; Serella, in 1868; Woodward, in 1881; Lampadorius, in 1891. These men all believed that, when the pressure was reduced and the temperature lowered, the body became "markedly exhausted," with the production of rheumatic and neuralgic symptoms. Also, according to this theory, spinal cord symptoms resulted from a reflex produced by "spontaneous refrigeration."

The theory of mechanical congestion was based on the assumption that when the body was exposed to increased air pressure, the peripheral vessels collapsed and the blood was driven into the visceral organs, particularly those which were protected by bone, that is, the brain and spinal cord. It is interesting to note that the proponents of this theory linked the sequelae to the cause. They named five sequelae: first, "black blood"; second, "evolution of gas"; third, "hemorrhage"; fourth, "acute revulsive anemia"; fifth, "comparative stasis." By "black blood" was meant blood deprived of its oxygen, which, because of its retention in congested internal organs, produced a deteriorating effect upon the tissues of these organs. The second sequela, "evolution of gas," was proposed in 1861 by Boucquoy, who assumed that internal congestion followed by a sudden release of pressure resulted in the liberation of gas and that this was confined to the internal organs and tissues. This idea comes closest to the present-day gas-embolism theory. The third sequela, hemorrhage, was supposed to result from rupture of distended vessels, due to pressure of the blood forced in from the periphery. "Revulsive anemia" was explained as due to the blood passing from the congested internal organs to the empty external vessels upon rapid decompression, while "comparative stasis" was attributed to a paralysis from over-distention of the internal vessels.

The recent gas-embolism theory actually dates from the work of Robert Boyle, about 1662, who was the first to observe gas bubbles in the blood of animals subjected to suddenly decreased air pressure. Through the work of Bert, Hoppe-Seyler, Hill, McLeod (18), and others, it has been proved that the symptoms of caisson disease are produced by air or gas emboli. The fluids and tissues of a man working in compressed air become saturated with the gases of the atmosphere, the extent of the saturation depending upon the length of exposure to the increased pressure, the intensity of the pressure, and the vascularity and absorptive rates and capacities of the various tissues. Since 80 per cent of the atmosphere is made up of nitrogen, and since the fatty tissues are capable of absorbing about five times more nitrogen than the blood plasma or other tissues, it is obvious that the lipoid-containing tissues become the storehouses of nitrogen after prolonged exposure to compressed air. As the pressure is released, the tissues give up their nitrogen to the circulating blood, the blood in turn giving up its nitrogen to the outside air through the pulmonic capillaries. Those body tissues which have a copious circulation lose their gas rapidly and, even if gas bubbles appear in the vessels of these tissues, they may pass harmlessly through the capillary beds without producing infarction. The fat tissues, bone marrow, and white matter of the brain and cord, however, have a relatively poor blood supply in comparison with their bulk, and therefore cannot rid themselves of their nitrogen as readily as other tissues. This is particularly true of the fatty tissues, which contain a relatively larger amount of nitrogen. Small bubbles of gas occurring in these tissues are less rapidly carried away and may increase in size sufficiently to obstruct the capillaries.

This obstruction prevents further nitrogen absorption by the blood plasma, while continued release of the nitrogen in the tissues forces the gas to accumulate in the spaces about the capillaries. Not only do such gas accumulations render capillary obstruction more complete, but, as they increase in size, actual tissue rupture may occur.

When decompression takes place so rapidly as to prevent the carrying off of the nitrogen and other gases from the tissues, a symptom-complex known as "bends" results. The present study has shown, however, that a great many cases of aseptic necrosis in the long bones have occurred in compressed-air workers with no history of "bends." This indicates that the periods of exposure to compressed air have been short enough, and the periods of decompression have been long enough, to prevent the occurrence of emboli or damaging extravascular nitrogen accumulations in the spinal cord or other non-osseous tissues. It also indicates that in spite of the failure of these infarcts to appear in the general tissues, they have nevertheless occurred in the bone marrow.

Experimentally, Kahlstrom, Burton, and Phemister (15, 16) have shown that the injection of air into the nutrient artery of a long bone fails to produce a lesion of the type found in caisson disease. In fact, though an infarct develops under such circumstances, the results indicate that there is more in the production of the bone infarct of caisson disease than simply the freeing of gas in the nutrient artery. For these reasons, additional factors are necessary to explain the prevalence of these necroses, or infarcts, in the bones of compressed-air workers who have never had symptoms of "bends." We believe that these factors are to be found in the anatomy and histology of the major long bones. In the first place, the bones are fixed, non-expansile structures with the nutrient foramina and their blood vessels as the only communicating paths between the marrow and outside tissues. Furthermore, the marrow of the major long bones contains a large amount of fat. In an adult, there are found in these bones only two small areas of red marrow, one in the upper end of the shaft of the femur and the other in the upper end of the shaft of the humerus. Elsewhere in the long bones of the extremities the red marrow has been almost entirely replaced by yellow marrow of high fat content. The femora are known to contain about two-thirds of the total yellow fat marrow. Of the remaining third, the humeri contain the largest amount, and the tibiae, fibulae, radii, and ulnae practically all of the rest.

The marrow of the long bones and the cancellous tissues at their extremities, particularly the upper extremity of the femur and the upper extremity of the humerus, all have a rather poor and sluggish circulation. During decompression, the relatively large amount of nitrogen stored up in the marrow fat and the smaller amount of nitrogen tied up in other marrow structures must be carried off by the circulation as rapidly as it is freed. The mechanism in the general fatty tissues and the white matter of the brain and cord is, of course, the same, and these tissues are similarly susceptible, because of sluggishness of their circulation, to the accumulation of bubbles in the capillaries. In them, also, perivascular gas accumulations may occur if the nitrogen is freed from the tissues more rapidly than it can be absorbed and carried away by the blood stream. In the long bones, however, there exists one additional factor, that is non-expansibility. As extravascular gas accumulations occur, capillary obstruction is much more likely to take place in non-expansile structures than in the expansile structures, where an increase in the volume of tissue because of the presence of gas results simply in the displacement of the vessels without actual compression.

The circulation in the marrow of the long bones is now fairly well understood, but the head of the femur is an exception. It is generally accepted that its blood supply is maintained from three sources: first, the artery of the ligamentum teres;

second, the vessels of the capsule, particularly the posterior capsular artery through the cortical perforations at the attachment of the capsule; third, the vessels entering the head through the marrow from the main nutrient artery of the shaft. At present, it is thought that in the adult femur the blood supply through the ligamentum teres is inadequate, and that the capsular branches are the most important source. The question arises whether there is any definite anastomosis between the capsular branches and the marrow vessels, or whether each has its separate terminal circulation. Drinker and Lund (9) have shown that there is a definite but variable degree of anastomosis between the diaphyseal and epiphyseal vessels in the adult laboratory animal, but this does not indicate that the same condition obtains in the human being. Many authorities believe that while in some persons there is no anastomosis between the marrow, capsular, and ligamentum teres circulations, in others there may be a significant amount. In this connection it should be stated that the degree of collateral circulation in the head of the femur varies in the same individual on the two sides, and also with age. Only such variations in the normal can explain individual differences, in youth or in advanced age, in union of fractures of the neck of the femur and the progression of aseptic necrosis in this area. While there is a variation in the degree of anastomosis of the three circulations, it is obvious from the work of many investigators that no single one of these is sufficient to maintain a normal condition of the bone and, therefore, from a practical standpoint, the circulation of the head and neck of the femur can be regarded as terminal.

The circulation in the humerus is in some respects similar to that of the femur, except that in the head of the humerus we have to consider only the anastomosis between the nutrient artery and the capsular branches. Here, also, in view of the varying degree of anastomosis between the nutrient artery of the shaft and the capsular branches, the circulation of the head is for all practical purposes a terminal one.

In addition to the circulation through the nutrient artery and capsule, all of the long bones contain a collateral circulation of varying degree from the periosteum through the haversian system. Here again the amount of anastomosis thus obtained is usually inadequate except for the needs of the periosteum, cortex, and endosteum.

Boyd (4), in his *Pathology of Internal Diseases*, makes a statement which is of interest in the consideration of the circulation in the long bone marrow, and the possibility of the occurrence of gas infarcts in this tissue. He has observed a liquefaction of the fat in the femur and tibia in two cases of chronic alcoholism which he studied at autopsy. On trephining these bones, the marrow fat ran out in a liquid state, indicating that marked fatty tissue degeneration had occurred. Boyd does not state what degree of alcoholism is required to produce this degeneration, but it may be assumed that where such degeneration takes place, marrow circulation has been impaired. It would thus be reasonable to suppose that in chronic alcoholics, where fat degeneration and liquefaction had occurred, infarct from nitrogen emboli and extravascular nitrogen accumulations would be a probable concurrent condition. One of the oddities of compression work is the fact that on decompression the worker complains of an abnormal thirst. In many instances this thirst is quenched by beer or liquids of higher alcoholic content, and the use of alcohol among these workers may, therefore, be assumed to be greater than for the average worker. This may well be a factor in the large incidence of bone necroses in compressed-air workers.

PRESENT STUDY

Through arrangements made by a member of the New York State Department of Labor, we were able to make an extensive x-ray study of 32 compressed-air workers, none of whom admitted the presence of skeletal symptoms. One of the conditions

imposed in conducting this study was that no historical data with regard to the pressures to which the workers had been subjected, previous illnesses, age, nationality, number of decompressions, etc., were to be ascertained from the patients. The x-ray study included examinations of the skull, both shoulders and upper humeri, both elbows and lower humeri, one hand, both hips and upper femora, and both knee joints including the adjacent portions of the femora, tibiae, and fibulae.

Such histories as were permitted indicated that the men had all worked intermittently for from three to thirty-three years in compressed air. The shortest single period of continuous employment was ten months, and the longest single period of continuous employment was thirty-six months. Of the total number examined, 14 (44 per cent) gave a definite history of having had "bends," 1 had had a single attack of otalgia, and 4 who had no history of "bends" stated that they had had attacks of arthritis. It should be noted that some of the patients giving a positive history of "bends" considered any myalgia or skeletal pain to be evidence of "bends," and in some instances that diagnosis was not justified by a close analysis of the symptoms. One of the men complaining of rheumatic attacks showed evidence of joint pathology due to compression, and one of those with arthritis showed evidence of compression disease in one hip and definite hypertrophic osteoarthritis in the other.

X-Ray Findings: The x-ray findings in this series differed in type according to location. In the shafts of the bones, areas of necrosis of varying sizes were seen in the medullary portion followed by calcification within and about the necrotic areas. The calcific areas were seen as strands of calcification running either along the endosteum or in the medullary portion; in some instances these coalesced into irregularly shaped dense masses. As the pathology became more marked, the calcific deposits were increased in amount and extent, but never extended beyond the metaphyseal portion of the bone. The areas of calcification most often did not follow the course of the bone trabeculae but ran either at right angles or obliquely to them. In the heads of the bones the early changes consisted in relative increases in density in the portion beneath the articular surface, an appearance described by Brailsford (5) as the first change in aseptic necrosis. The size of the dense area depended on the extent of the bone infarct. The increased density was greatest immediately adjacent to the articular margin, and as the disease progressed there was a further increase in density until small areas of necrosis appeared. The necrotic areas gradually increased in size but, after necrosis was once established, there was little change in density in the portions of the bone not involved in the necrosis. As these changes developed, thinning, irregularity and fragmentation about the articular margins and, finally, collapse of the joint surface took place.

With respect to the changes in the shafts of the long bones, we have classified these in three groups: first, necrosis without calcification, called one plus (Fig. 1); second, necrosis with early calcification, two plus (Fig. 2); third, marked calcific deposits, three plus (Fig. 3). The epiphyseal or head pathology was divided in four groups: first, relative increase in density, called one plus (Fig. 4); second, increase in the density with small areas of necrosis, two plus (Fig. 5); third, large areas of necrosis with relatively less increase in density and also possible cartilaginous changes, three plus (Fig. 6); and fourth, collapse and fragmentation of the articular surface, four plus (Fig. 7).

Of the total of 32 cases in this investigation, only 8 failed to show bone or joint changes considered to be typical and characteristic. In other words, 75 per cent showed positive changes in one or more bones on x-ray examination.

The bones involved in the cases studied were the femora, humeri, tibiae, and fibulae (Table I). The femora were involved in 21 of the cases, the humeri in 17, the tibiae

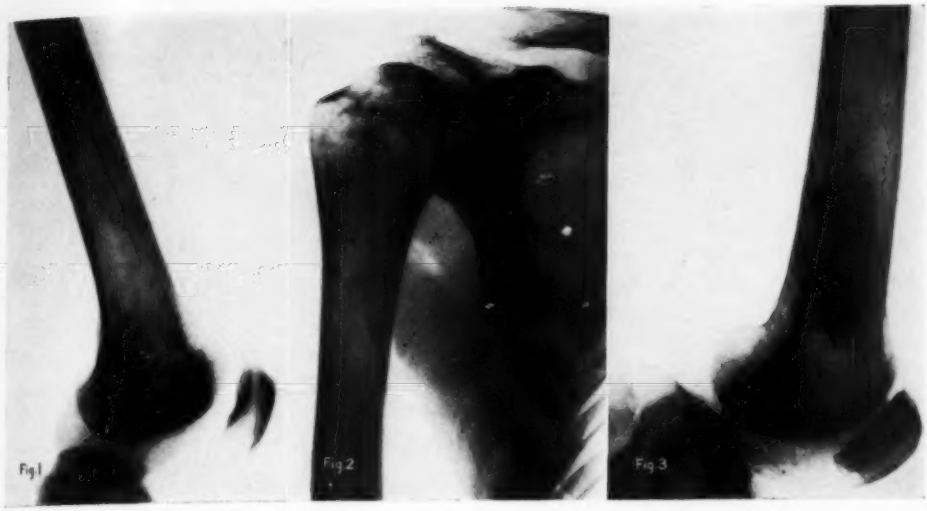

Fig. 1. Large area of aseptic necrosis in the shaft of the femur without evidence of calcification in the major portion of the lesion.
Fig. 2. Large area of aseptic necrosis in the upper portion of the shaft of the humerus with almost complete marginal calcification.
Fig. 3. Large area of calcification in the lower portion of the shaft of the femur almost completely filling the old necrotic area.

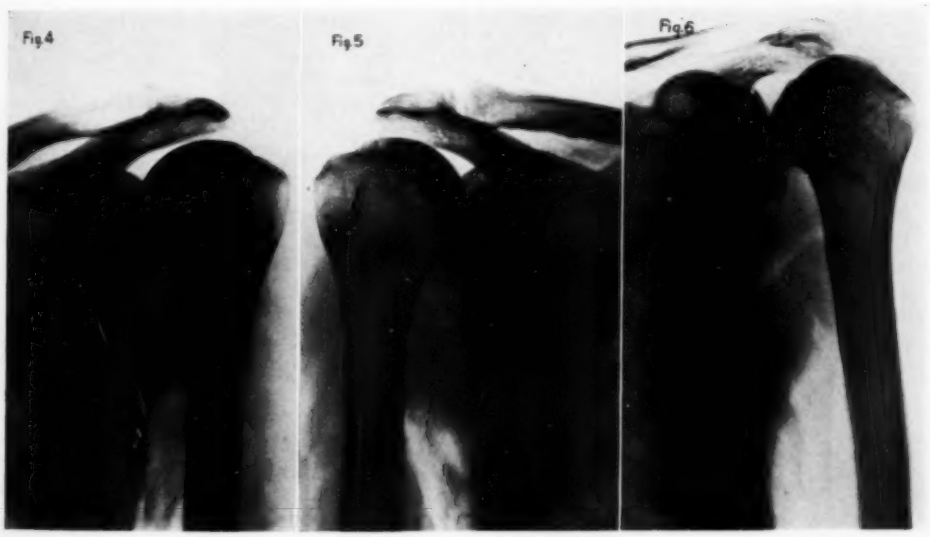

Fig. 4. Relative increase in density of a part of the head of the humerus representing the first stage of epiphyseal infarction.
Fig. 5. Increased density in the head of the humerus with areas of beginning necrosis within the dense area.
Fig. 6. Large areas of necrosis and beginning changes in the articular surface of the head of the humerus. Areas of increased density are still present.

TABLE I: DISTRIBUTION OF BONE CHANGES

Case No.	R. Hum. Head	L. Hum. Head	R. Hum. Shaft	L. Hum. Shaft	R. Fem. Head	L. Fem. Head	R. Fem. Shaft	L. Fem. Shaft	R. Tib.	L. Tib.	Fib.
34	0	0	0	0	0	0	++	++	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0
35	+	0	++	++	0	0	++	+++	+++	+++	0
8	++	++	0	++	+	+	++	0	0	0	0
5	++	++	0	0	++	+	+++	+++	++	++	0
28	0	0	0	0	0	0	0	0	0	0	0
50	0	0	++	++	+	0	++++	0	++	0	0
7	0	0	+	0	0	0	++	++	++	0	0
20A	0	+++	++	+++	0	++++	+++	+++	+++	+++	+++
4	0	++++	0	+++	+++	0	0	0	0	0	0
40	0	0	++	0	0	0	0	0	0	0	0
39	0	++++	0	0	0	0	0	++	0	0	0
33	0	0	0	0	0	0	0	+++	0	0	0
11	+	0	0	0	0	+++	++	++	0	0	0
10	++	0	0	0	0	0	++++	0	0	0	0
24	++	++	++	++	0	0	0	0	0	0	0
23	0	+	0	++	0	0	++	++	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	+	0	0	0	0
25	0	0	0	0	0	0	+	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	+	0	++	++	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0
12	++++	++	+++	0	++	++	+++	+++	0	0	0
21A	0	++++	0	+	++++	0	0	0	0	0	0
13	++++	++++	+++	+++	++++	++++	+	+	0	0	0
1	0	++++	0	+	0	++++	++	0	0	0	0
2	0	0	0	0	++	0	0	0	0	0	0
27	0	0	0	0	0	+	0	0	0	0	0

in 5, and the fibulae in 1. Of the 24 positive cases, 16 showed positive shaft and head changes, 6 showed positive shaft changes with negative epiphyses, and only 2 showed positive changes in the heads with negative shafts. Eighteen of the cases showed involvement of more than one bone.

In our cases of positive shaft pathology we noted a degree of change proportionate to the years of employment at compressed-air work. The changes were also proportionately influenced by the length of consecutive periods of employment (Table II). The men with a one-plus change in the shafts showed an average of 13.1 years of employment and an average of 19 months of consecutive employment. Those with a two-plus change showed an average of 19.3 years of employment with an average of 26 months of consecutive employment. Those with a three-plus change showed an average of 25.7 years of employment with an average of 31 months of consecutive employment. Of the men showing changes in the heads of the bones, those with a one-plus change had an average of 22 years of employment with 26.5 months of consecutive employment; those with a two-plus change, 24.7 years of employment with 27.3 months of consecutive employment; while those with three-plus changes averaged 22.5 years of employment with an average of 27 months of consecutive employment. With four-plus change the average was 18.5 years of employment and 20.6 months of consecutive employment. These observations are illustrated in the accompanying graphs (Fig. 8).

An analysis of these graphs indicates that, as the years of total employment increased and the periods of consecutive employment lengthened, the changes in the shafts increased progressively. On the other hand, it is to be noted that in the heads of the bones the one- and two-plus changes showed proportionate increases in length of employment and periods of

TABLE II: YEARS OF EMPLOYMENT AND MONTHS OF CONSECUTIVE EMPLOYMENT IN CASES WITH AND WITHOUT BONE CHANGES

ANALYSIS OF CASES WITHOUT BONE CHANGES

Case No.	Years Employed	Months of Continuous Employment	History of "Bends"
38	15	18	neg.
28	5	12	???
31	No data	No data	No data
6	15	12	pos.
30	14	18	pos.
14	22	24	pos.
20	3	16	neg.
9	16	18	???
Average	12.8	16.8	

62.5% positive or questionable history of "bends."

ANALYSIS OF CASES WITH BONE CHANGES*

Case No.	Years Employed	Months of Continuous Employment	History of "Bends"
35	25	36	pos.
8	30	36	neg.
5	25	24	pos.
4	25	36	pos.
39	13	24	neg.
11	20	18	pos.
10	20	18	pos.
24	13	24	neg.
23	15	18	???
12	33	36	pos.
13	14	18	pos.
1	20	18	pos.
50	No data	No data	No data
20 A	No data	No data	No data
21 A	No data	No data	No data
7	14	30	pos.
26	14	12	neg.
25	3	18	neg.
34	12	18	neg.
40	10	18	???
19	No data	No data	No data
27	9	18	???
2	17	10	pos.
33	20	24	neg.
Average	17.6	22.7	

54% positive or questionable history of "bends."

* Historical data, other than those cited above, were denied to the authors in this investigation.

consecutive employment, but the three- and four-plus changes showed approximately the same length of employment. Only two of the men with positive findings showed changes in the head without changes in the shaft, so that it is reasonable to assume that the majority of those developing infarcts in the heads of the bones became incapacitated at a relatively early period after such infarct and, therefore, the changes in the shafts, which require a longer period for their development, had not as yet appeared as strikingly as where no involvement, or only slight involvement, of the heads of the bones had occurred.

There is one other significant factor with regard to those persons showing marked changes in the heads of the bones. It will be noted from the above figures that the shortest period of consecutive employment for even the one-plus changes was 26.5 months, and the average period of consecutive employment for all cases of involvement of the heads of the bones was 26.9 months. In comparison with this figure, the average period of consecutive employment in those showing shaft changes was 25.3 months. These figures are not in themselves striking but, even in this small series, indicate that long periods of consecutive employment may be factors in the production of changes in the heads of the bones.

Fig. 7. Collapse and fragmentation of the articular surface of the upper extremity of the humerus.

CONCLUSIONS

1. We believe that the changes described above are pathognomonic of bone

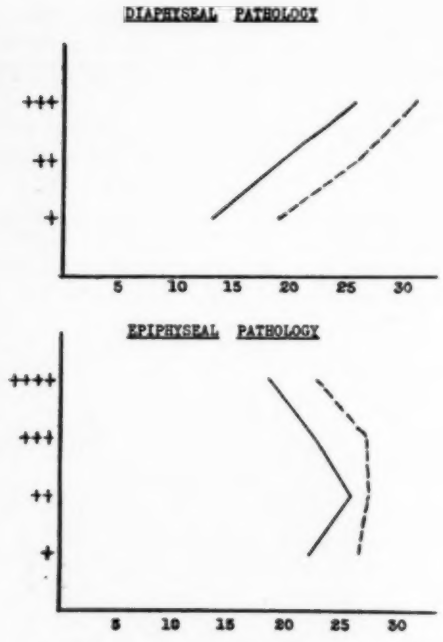

Fig. 8. Graphs representing the relationship of years of employment and months of consecutive employment to the degree of diaphyseal and epiphyseal pathology. The solid lines represent years of employment, the dash lines months of consecutive employment.

necrosis due to employment in compressed air. This is particularly true where the changes involve more than one bone and/or more than one area in the same bone. Of all cases studied, 75 per cent showed such changes.

2. The involvement of the various long bones is directly proportionate to their fat marrow content.

3. The changes in a large percentage of cases occurred in workers who had never had the "bends."

4. It is assumed that the changes are due to frequent and inadequate decompressions or denitrogenizations, resulting in cumulative nitrogen gas formation and consequent infarctions.

5. This study, though based on a small number of cases, indicates that a large percentage of compressed-air workers show this pathology, and points to the necessity for further studies on larger groups, preferably where adequate histories are obtainable.

6. Animal research should be instituted in order to ascertain the causative factors involved, and also to secure information as to methods of prevention.

Long Island College Hospital
Brooklyn, N. Y.

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Roentgen Sign of Early Suppurative Arthritis of the Hip in Infancy[1]

L. K. CHONT, M.D.
Oklahoma City, Oklahoma

DISEASES OF THE locomotor system, with the exception of chronic arthritis, are more common in childhood than in adults, and the symptoms are usually quite different than in later life. This is especially true in infancy, when the blood supply to the epiphyses and the osseous development are greater than at any other period in extra-uterine life.

Anatomically the infantile hip joint is composed of a very shallow, almost rimless acetabulum, a weak, thin joint capsule, and immature ligaments. The joint cartilages, on the other hand, particularly that of the femoral head, are much thicker than those of an adult hip. This thicker cartilage is an important protective factor against infectious processes of the joint, since it can resist destruction longer than a thin cartilage and thus allows time for surgical intervention.

The causative agents of secondary suppurative arthritis are restricted to pyogenic organisms: namely, streptococcus, staphylococcus, pneumococcus, meningococcus, and gonococcus. According to Smith, Gallup, and Osgood (2), streptococcal and meningococcal arthritides are more common under two years of age. Staphylococcic arthritis occurs usually in older children, while meningococcal and gonococcal arthritides have no predominance as to age group distribution.

Among the etiological factors, upper respiratory infections, sometimes very mild, and insignificant looking furuncles located either close to or distant from the involved hip are common. Many times only the most attentive questioning of the parents can recall these trivial lesions which may have occurred, and probably healed, days prior to the onset of hip symptoms. In other cases there is a preceding history of bronchopneumonia, lobar pneumonia, osteomyelitis, or meningitis. There is at least one report in the literature (1) of an infectious arthritis of the left hip following circumcision of a newborn infant. Of our 6 patients, 3 had infections of the respiratory system. One of them had bronchitis, another lobar pneumonia, and the third bronchopneumonia prior to the onset of coxitis. In Cases 4 and 5, the hip lesions were secondary to pneumococcal meningitis and furuncle, respectively, while in Case 6 no history of a preceding illness or lesion was obtained.

Since the infection is blood-borne, the general clinical symptoms are those of toxemia: increasing prostration, fever, and leukocytosis. The local symptoms consist of pain, swelling, and impaired function of the hip followed by muscle spasm, loss of the gluteal fold, and flexion of the thigh. In our cases the temperature varied between 101 and 105.8°, with an average of 103.2°. The red blood cells varied from 1,000,000 to 3,890,000, averaging 2,791,667, and the white cell count between 10,900 and 30,800, with an average of 17,316. All of these clinical symptoms and signs may occur in periarthritis, toxic or allergic reactions of the joint, nonpurulent synovitis, and osteomyelitis of the upper part of the femur or the periacetabular region of the pelvic bones.

The pathological process in a blood-borne suppurative arthritis of the hip begins with an enhanced secretion of serum into the joint cavity, resulting in an increased intracapsular pressure. Due to the anatomical structure of the infantile hip joint, a lateral and upward subluxation or dislocation of the femoral head occurs.

[1] From the Department of Radiology (John E. Heatley, M.D., F.A.C.R., Director), University of Oklahoma Medical School and Hospitals. Accepted for publication in February 1942.

Later, the increased synovial fluid becomes purulent and destroys the articular cartilages, resulting in ankylosis or telescoping of the hip.

Early diagnosis of these cases is essential to prevent permanent crippling of the child. Theoretically, aspiration of the joint can serve as a differential diagnostic aid in true intracapsular cases, but when the infection is periarticular, a careless aspiration might inoculate the joint cavity. Roentgen examination, on the other hand, not only is a safe diagnostic procedure but also gives reliable information as to the extent of the disease and the approximate amount of intracapsular fluid. Furthermore, it will differentiate a true infectious arthritis from an allergic one due either to a systemic disease or to a localized lesion, since in the latter the roentgen findings are negative. In view of the weak, undeveloped structures of the infantile hip joint, and the early pathology, which consists in the increased secretion of fluid into the joint capsule, it is evident that displacement of the femoral head will occur. Because, particularly in infancy, the least resistant part of the joint is the lateral wall of the articular capsule, this displacement will be lateral. The ever-present muscle spasm resulting from local inflammation will further elevate the femoral head. This lateral and upward displacement of the head of the femur is the pathognomonic sign of an early infectious arthritis of the infantile hip. This phenomenon is demonstrated well by a properly taken roentgenogram. To secure a reliable film the child should lie flat on his back and the tube should be centered in the mid-line. Both hips should be shown on the roentgenogram for comparison.

Fig. 1. Case 1: Marked lateral and upward displacement of the left femur. Femoral head is absent.

CASE REPORTS

CASE 1 (Hospital No. 100,124): L. V. L., white female, aged two months, had an upper respiratory infection about ten days prior to admission. Four days later she awakened crying, with the left leg flexed to the abdomen; attempts to straighten it caused her to cry, and the following morning the parents noticed that the left hip was swollen. The local physician referred the child to the hospital with a diagnosis of tuberculosis of the hip.

The red blood count was 2,310,000; hemoglobin 45 per cent (Sahli); white blood count 30,800; polymorphonuclears 80 per cent. Roentgen examination showed absence of the head of the left femur and displacement of the femoral neck laterally and upward. There was a marked soft tissue swelling around the left hip. Aspiration yielded thick yellow pus which showed streptococci growing in short chains. A posterior capsulotomy was done and the patient made an uneventful recovery.

CASE 2 (Hospital No. 100,359): B. L. J., colored female, aged four months, was admitted on Feb. 10, 1939. She had been well prior to the last week in January, when she had a rather mild pneumonia. After this a painful swelling developed in the region of the right upper thigh and hip, followed by fever and vomiting. A local physician incised the thigh, but only blood was obtained. No further treatment had been given. There was a positive history of syphilis in both parents.

On examination the child appeared well developed and well nourished, but markedly anemic. The orthopedic abnormality was confined to the region of the right hip and thigh; these areas were swollen and indurated, with increased local heat. Any pressure on or movement of the right thigh or hip caused extreme distress. The knee was maintained in flexion and the thigh abducted and rotated externally.

Roentgen study revealed a destructive process with periosteal elevation of the neck and upper two-thirds of the shaft of the right femur; a lateral subluxation of the femoral head with marked widening of joint space was present.

The red blood count was 2,600,000; hemoglobin 36 per cent (Sahli); white blood count 15,300, with neutrophils 64 per cent. A culture of aspirated material showed staphylococci.

Fig. 2. Case 2: Lateral and upward displacement of right femur; extensive destruction of femoral neck and head; periosteal elevation along upper shaft.

Traction was applied. Two weeks later a small incision was made over the lateral aspect of the thigh and over 100 c.c. of thick, dirty, grayish, purulent material was evacuated.

The patient made a slow but uneventful recovery. Two years later she walked with a slight limp on the right, and operation was advised.

CASE 3 (Hospital No. 105,215): J. W. L., a fourteen-month-old white boy, entered the hospital on March 16, 1940. Three weeks prior to admission he had an upper respiratory infection and bronchopneumonia. Ten days later he complained of pain in the right hip and refused to walk. For one week he had a fever of 102° and was restless. The right hip was flexed.

The child was fairly well developed, well nourished, and subacutely ill, with a temperature of 101°. His right hip was held in adduction and flexion, and any attempt at motion caused him to cry. The right greater trochanter was at a higher level than the left; there was a suggestion of fullness but no fluctuation about the hip joint.

The red blood count was 3,500,000; hemoglobin 60 per cent (Sahli); white count 10,700, with neutrophils 63 per cent. The tuberculin test and Kline and Wassermann tests were negative.

Roentgen examination showed a lateral subluxa-

tion of the right hip joint with the femoral head pointing to the most lateral part of the acetabulum. Aspiration of the right hip yielded about 0.5 c.c. of purulent material, which was negative for organisms in both smear and culture.

The patient was placed in traction. The swelling and tenderness about the right hip subsided and the temperature returned to normal. The x-ray picture taken 10 days after aspiration of the hip joint showed the femoral head to be well in the acetabulum. Three weeks after discharge, and again five weeks later, the child was playing and running, and had no limp.

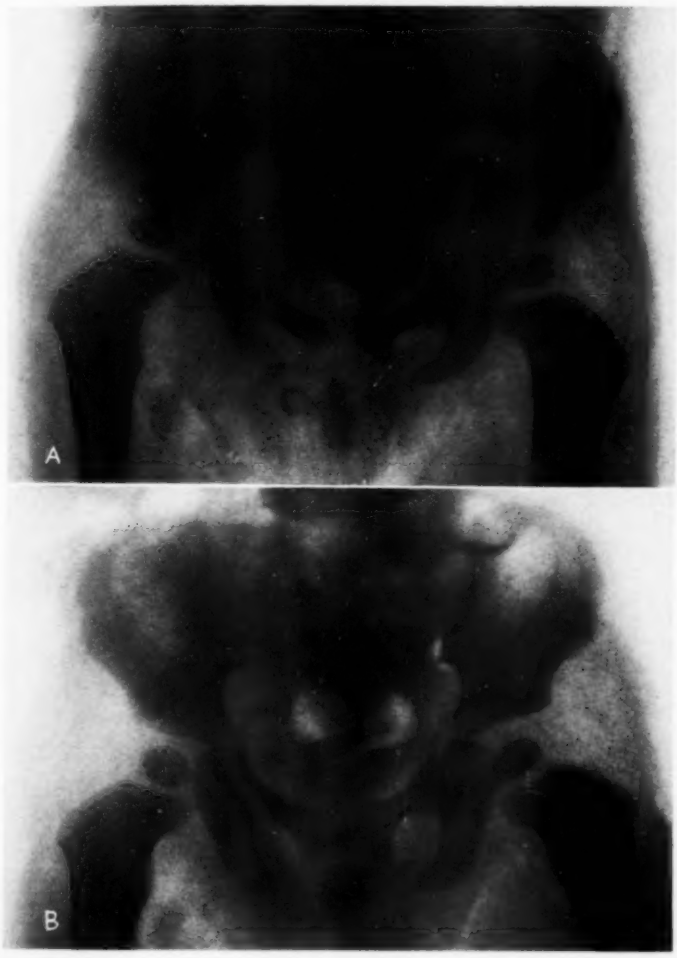

Fig. 3. Case 3: A. Lateral and upward displacement of right femur. B. Same case ten days after aspiration of joint. Femoral head is in a normal position.

CASE 4 (Hospital No. 99,323): G. A. B., a seven-month-old white girl, was brought to the outpatient department because of swelling in the knee joint and gums. On the first visit the temperature was normal but the baby appeared to be irritable and complained when moved or when pressure was made over the femora. Since she had never received an adequate amount of vitamin C in the diet, and because of physical findings, a tentative diagnosis of scurvy was made and dietary correction advised. X-ray examination of the femora was negative and failed to confirm the diagnosis of scurvy.

The patient was again brought to the hospital two days later, at which time the swelling about the left knee joint had decreased. She was less irritable, but had a temperature of 102°. Hospitalization

Fig. 4. Case 4: Marked lateral and slight upward displacement of left femur.

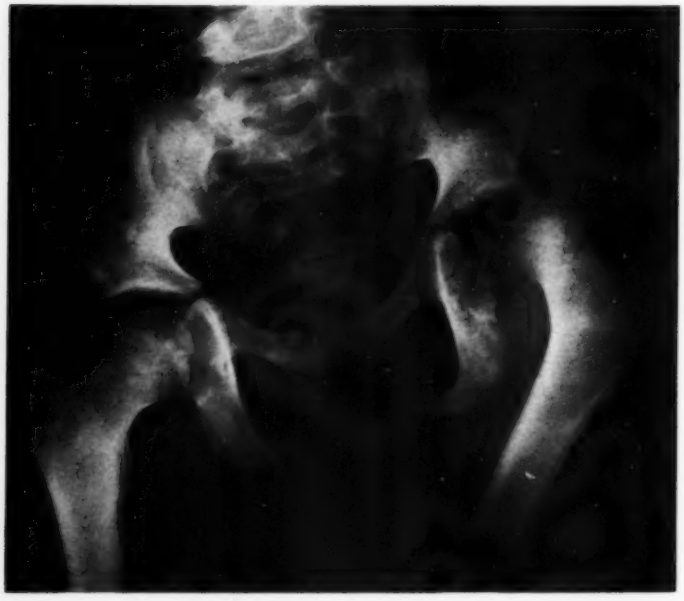

Fig. 5. Case 5: Subluxation of left hip; several small areas of destruction at lower half of acetabulum.

was advised, but the parents were reluctant to consent to this. Two days later, when the child was finally admitted, there were definite signs of involvement of the left lower extremity and a tentative diagnosis of osteomyelitis of the left femur was made.

The red blood count was 3,890,000; hemoglobin 80 per cent (Sahli); white blood count 11,900, with 42 per cent neutrophils. Kline test negative.

A roentgenogram taken at this time showed a lateral displacement of the left femoral head with widening of the joint space. The joint was aspirated, and the material obtained showed a mixed infection with Gram-positive diplococci and staphylococci. The condition did not improve after operation and the following day opisthotonos was present. Spinal puncture showed pneumococci, type three. Sulfanilamide was administered, as no specific serum was available, but the temperature continued high and death occurred. Permission for autopsy was not granted.

CASE 5 (Hospital No. 103,749): C. L., six-year-old white boy, was admitted to the hospital on Nov. 7, 1939. A little over three weeks prior to admission the parents noticed a furuncle on the right leg, at about the mid-thigh. It healed without giving any apparent trouble, but within a few days the patient complained of pain in the region of the left knee. The next day there was pain in the left hip, the boy was unable to walk, and a high fever was present. A posterior arthrotomy was done at a local hospital but the condition did not improve, and the child was brought to our hospital.

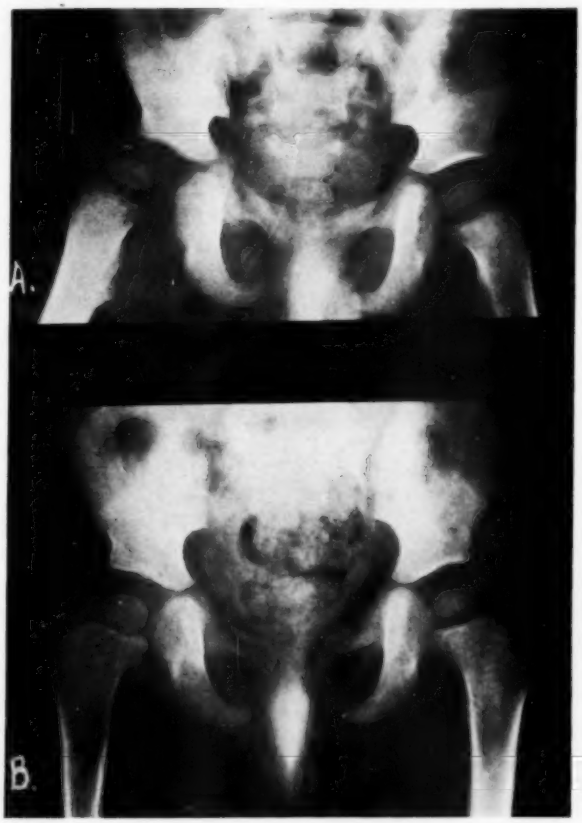

Fig. 6. Case 6: A. Lateral and upward displacement of right femur. B. Same case after aspiration of joint.

The patient was acutely ill, very anemic, and greatly emaciated. The mucous membranes were pale and dehydrated. There was a subluxation of the left hip. The greater trochanter was prominent and the whole leg was internally rotated and adducted. There was very little swelling about the left hip, but a fairly profuse amount of thick, yellow, purulent material was obtained from surgical incision over the posterior aspect.

X-ray studies showed subluxation of the left hip and an early destructive process around the inferior portion of the acetabulum. Because the red blood count was very low (1,000,000 with 33 per cent hemoglobin) a blood transfusion was given at once and the subluxation was treated conservatively. A roentgenogram taken two days later showed the subluxation to be reduced, and the general condition improved following the transfusion.

The red blood cells numbered 1,000,000; hemoglobin 33 per cent; white blood count 12,200, with 72 per cent polymorphonuclears. Blood culture was sterile after ten days.

CASE 6 (Hospital No. 100,599): C. P., a sixteen-month-old white boy, was admitted to the hospital on March 1, 1939. He had been apparently well until five days prior to admission, at which time the parents noticed that he was beginning to limp a little and showed unwillingness to stand on the right leg. Subsequent to this, the upper right leg became swollen and tender. When seen in the out-patient department the child had a temperature of 104.2°, and there were increased heat, thickening, and marked tenderness about the right hip, which was held in flexion.

Roentgen examination showed a marked widening of the right hip joint with lateral displacement of the femur.

The red blood count was 3,450,000; hemoglobin 75 per cent (Sahli); white blood count 23,000, with polymorphonuclears 82 per cent.

Under general anesthesia a posterior arthrotomy was done, and about one and one-half ounces of thick yellow pus were obtained. Smear and culture revealed Gram-negative diplococci. Recovery was uneventful.

SUMMARY

1. Diseases of the locomotor system are more common in childhood than in later life and differ from those in adults.

2. Streptococcal and meningococcal arthritides occur more frequently in patients under two years of age.

3. Early suppurative arthritis may result from even a mild upper respiratory infection, an insignificant furuncle, pneumonia, osteomyelitis, or meningitis.

4. The infection being blood-borne, the general clinical symptoms are those of a toxemia.

5. Because of the anatomical structure of the infantile hip joint and the greatly increased intracapsular fluid, a lateral and upward subluxation or dislocation of the femoral head occurs.

6. The increased synovial fluid becomes purulent, destroys the articular cartilages, and a permanent crippling results if surgical intervention is delayed.

7. Roentgen examination is a reliable diagnostic procedure, revealing, also, the extent of the disease and the amount of intracapsular fluid present. It will further differentiate a true infectious arthritis of the infantile hip.

600 Osler Building
Oklahoma City, Oklahoma

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A Simple Calculator for Therapy Exposure Times[1]

LEWIS G. JACOBS, M.D.

Indianapolis, Indiana

NOMOGRAPHS for making various calculations are no novelty, but since the technic of constructing this form of chart is not known to many physicians, a nomograph for calculating therapy exposures is here presented. This chart will give the correct exposure time for any dose within its range for various technics, which may be almost unlimited in number, and for various focus-skin distances. The most important advantage of such a chart is the protection it affords from errors in arithmetic, since it supplants all other calculations and requires only a single setting of a sliding scale and a stretch of a string across from the dose scale through the distance scale to the time scale, where the answer may be read.

Figure 1 shows a completed nomograph arranged for the technics and distances used in this office. The arrow is set to point to the technic in use, and the string carried on stretch from the dose to be given through the distance used[2] to the time scale, where the exposure time is read.

While the theory which explains the operation of this chart is not extremely complex, it is of no great interest here. In constructing the chart, the three scales must be made parallel and equidistant. The choice of the center as the sliding scale in preference to one of the others is merely a matter of convenience of construction. All of the scales are identical, being simple logarithmic scales (1 cycle = 5 inches). Such scales may be found in the single scale of a 5-inch slide rule or on many types of 2-cycle semilog graph paper. The range of dose is a matter of choice; it can be carried over any chosen range. We preferred 20 to 2,000 r.

The time scale will in general cover a corresponding range. It is desirable to have a double marking on the time scale, one side being graduated in minutes and the other in seconds. If one starts, as we do, at 1/2 minute, the second scale will start at 30; the markings will be found to correspond exactly; that is, if 30 is placed opposite 1/2, 60 will be opposite 1, 90 opposite 1 1/2, 120 opposite 2, etc. This peculiarity is inherent in the log scale. The time scale must be in the opposite direction from the dose scale; that is, if the dose scale readings decrease from top to bottom the time scale readings must increase from top to bottom.

The sliding (distance) scale is plotted in exactly the same manner, choosing any distances desired and directing the scale the same as the time scale. On one side of the slide an arrow is drawn. It is convenient to plot the slide on a sheet of celluloid into which a slot has been cut parallel to the scale. The mounting on the finished graph is accomplished by fastening two clips through this slot and the backing of the graph so as to place the scale properly.

On a small separate sheet the technics to be used are plotted in the following manner: a list of the outputs in r/min. for each technic is made; it is immaterial at what distance these outputs are taken, as long as the distance is the same for all technics. These outputs are next plotted on a 2 1/2-inch log scale (this is the double scale of a 5-inch slide rule or one cycle of most 4-cycle semilog graph papers) and each mark is labelled with the voltage and filter to which it corresponds. These plot marks are best made lines, to which the arrow may be aligned. The sheet is then mounted on the graph in the following manner, and it is of the utmost importance that it be accurately done. The distance

[1] Accepted for publication in January 1942.

[2] We prefer to measure distance in inches, but centimeters or any other regular scale may be used; two scales can be placed on opposite sides of the ruling.

scale is so set that the readings correspond to those that would be proper for one of the technics. This involves a longhand calculation for some one set—technic, distance, dose, and time. When the slide scale is so set, the insert with the technic if they are exactly accurate the graph will be also. The advantage of having the scales for short times and for small doses on a larger spread than those for longer times or larger doses is obvious, and of course the log scale has this characteristic.

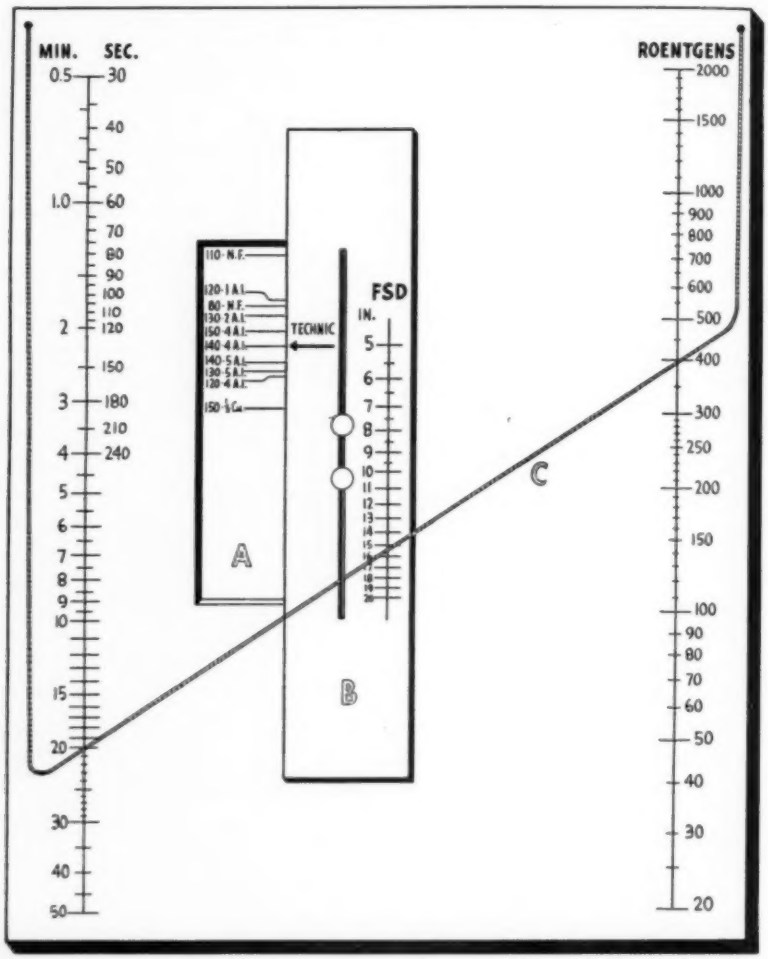

Fig. 1. Calculator calibrated for our office technics. A. Insert with outputs in r/min. plotted on it, placed in position. B. Sliding scale for distances. C. Thread on stretch.

lines is mounted with the mark for the technic so used opposite the arrow. All technics will then be in proper position, although it is wise to run a few check calculations to rule out errors in plotting or arithmetic. The nomograph will be only as accurate as the scales themselves; Each time the calibration is changed the technic insert must be changed also; this is done by making a new insert in the same manner that the original insert was made.

For those unfamiliar with the properties of logarithmic scales, they are so arranged that each cycle represents a factor of 10

times; when the end mark of 1 (or 10 or 100 or 1,000) is reached, the scale is prolonged by repeating the same scale, multiplying the numbers on it by 10. In other words, the 1–10 scale is the same as the 10–100 scale, 2 corresponding to 20 and 3 to 30, etc.

Once constructed, this chart can be used by anyone after brief instruction, and may either form a check on the calculations of exposure time or be the sole method of such calculations. If the settings are chosen correctly, the chart will be accurate.

23 East Ohio St., Indianapolis, Ind.

Radiation Effects on the Blood Vessels[1]

Part III: Telangiectasis; Effects on Lymph Vessels

J. BORAK, M.D.

Lecturer on Radiology, New York University, School of Medicine

TELANGIECTASIS

TELANGIECTASIS is a vascular phenomenon second to the erythema in frequency of incidence. Microscopically the lesions have the appearance of tubes made up solely of endothelial cells, thus proving that we are dealing here with capillaries. These vessels differ from normal capillaries only in their increased caliber. This dilatation can be recognized microscopically before it has become visible clinically (Schugt, Löw-Beer and Redisch). According to Lewis, clinical visibility requires a lumen measuring at least 0.02 mm. Since normal capillaries measure only about 0.008 mm., the telangiectatic vessels are dilated as much as two and one-half times. It may be said, therefore, that in telangiectasis the capillaries attain the caliber of veins. At the same time the circulation is somewhat slowed, giving the vessels a bluish color. Two stages may be distinguished: a first stage in which the telangiectatic vessels are increasing in size and number and a second stage, lasting for years or even decades, in which they remain stationary. In most cases they appear as distinct individual vessels, but sometimes they fuse with one another, leading to a diffuse discoloration of the skin, as in an erythema.

According to Lewis, these vessels do not react to histamin, obviously because they have already reached the limit of dilatation. The permeability of the walls cannot be increased, so that neither an erythema nor formation of a wheal occurs. There is also no blanching of the telangiectatic skin in response to adrenalin, either given subcutaneously (Freund and Oppenheim; Siedamgrotzky) or directly into the ectatic vessels (Lewis). This indicates that the dilatation of the capillaries is not the result of a dilatation of the arterioles.

The outstanding difference between the radiation erythema and telangiectasis is the period of latency. This amounts to only a few hours or days in the case of erythema, while many months—in most cases about a year—elapse before telangiectasis makes its appearance. The explanation of this delayed manifestation is closely related to the origin of the telangiectasis. Several theories have been advanced. Kienböck regarded this phenomenon as the result of a shrinkage of the connective tissue surrounding the vessels. Freund and Oppenheim believed that telangiectasis develops like an aneurysm, due to damage to the capillary walls. Kok and Vorlaender were of the opinion that the active capillaries are destroyed and the reserve capillaries become telangiectatic as a compensation.

Kienböck's theory is not supported by the anatomical findings. In histologic sections of skin in which telangiectasis is manifest no signs of a perivascular edema or of inflammation and, more particularly, no adhesions between the vessels and the adjacent tissues, are to be seen. The theory of Freund and Oppenheim is likewise open to objection. The walls of the ectatic capillaries do not exhibit pathologic changes; the endothelial cells are not swollen, and there are no vacuoles or other signs of degeneration either in the protoplasm or in the nucleus. It may be added that in true aneurysms the dilatation occurs at the cost of the muscle and elastic tissues, which are entirely lacking in the capillaries.

With regard to the theory of Kok and Vorlaender, it should be remembered that the distinction between the active and resting capillaries which is valid for muscle tissue does not apply to the skin. Here the capillaries, as Lewis, Zweifach, and others have emphasized, are constantly functioning to a greater or less degree. There are

[1] Continued from May, page 617.

no capillaries in the skin which may be accurately designated as reserve capillaries.

A different conception as to the origin of telangiectasis is obtained when one analyzes not only the ectatic vessels, but also the vessels in their neighborhood. Cases are seen in which an ulcer occurs in the center of the irradiated field while telangiectasis develops in the periphery. Thus two opposite processes take place coincidentally in the blood vessels: obstruction in the center and dilatation in the periphery. This suggests the conclusion that the latter may be the result of the former. Further study of cases with telangiectasis corroborates the conception that its ultimate cause is to be sought in an obstacle to the flow of the venous blood. This obstacle in most cases is a fibrotic process in the intima of the veins situated in the deeper portion of the corium, a phlebofibrosis or phlebosclerosis.

In accordance with this fact, the ectatic vessels have been found to be "extraordinarily contorted" (Lewis), as is also the case in prolonged stenosis of other hollow organs, as for example the ureter or esophagus. Fahr, too, states expressly that, while the capillaries in the stratum papillare are strikingly dilated ". . . certain large veins show signs of thickening and sclerosis of their walls and a narrowing of the lumen, which frequently appears only as a narrow fissure." To this may be added the description of Freund and Oppenheim. According to them, "the greatest number of these gaps (telangiectases) is in the dense connective tissue directly under the papillary layer of the cutis." This distribution is quite typical. It is the subpapillary layer of the corium where the telangiectases are first found and where they are most pronounced and most abundant. Gradually the vessels in the more superficial layers of the corium become dilated, while, even in very pronounced cases, they are found only rarely in the subcutis.

The behavior of the arteries differs remarkably from that of the veins in telangiectasis. Gassmann, Thiess, and many others found the radiation effects to be, in general, more pronounced in the arteries. Windholz, as well as Brighton, Altmann and Hagan, however, found them more pronounced in the veins. One may conclude from this that there is no real difference in radiosensitivity between the two vessels, but that the results depend on certain other factors. One of these concerns the structure of the two vessels, another the mode of irradiation. Of the structural features, the fact that the arteries have a smaller lumen than the accompanying veins is of special importance. Thus, while a narrowing in the veins may lead merely to a dilatation of the prestenotic capillaries, that is, to telangiectasis, far more serious events may follow narrowing of the same degree in the lumen of the arteries. A complete occlusion may result, with consequent tissue necrosis. If the narrowing is less pronounced, fibroatrophy and depigmentation of the skin occur, which in a later stage may likewise be followed by necrosis.

Because, in such instances as have been mentioned, highly serious alterations of the skin are present, telangiectasis is usually considered an indicator of severe damage to the vessels and a forerunner of tissue necrosis. Actually there are many cases in which the arteries exhibit no changes at all or only those of mild character. In such cases, except for epilation of the irradiated area, no remarkable changes are observed. The fact that the veins in these cases are narrowed to a degree leading to the development of telangiectasis while the arteries, despite their smaller lumina, show no stenotic effect, is due in part to the higher blood pressure in the arteries and in part to their more abundant muscular elements. As a result of this difference in blood pressure and tonus, stenosis can be overcome much more readily in the arteries than in the veins. In addition, the veins contain more fibrous tissue than the arteries, and for this reason a fibrosis may develop to such an extent as to hinder the venous blood flow while the arteries are still unobstructed. This explains the fact that telangiectasis may exist without a noticeable disturbance of arterial circulation.

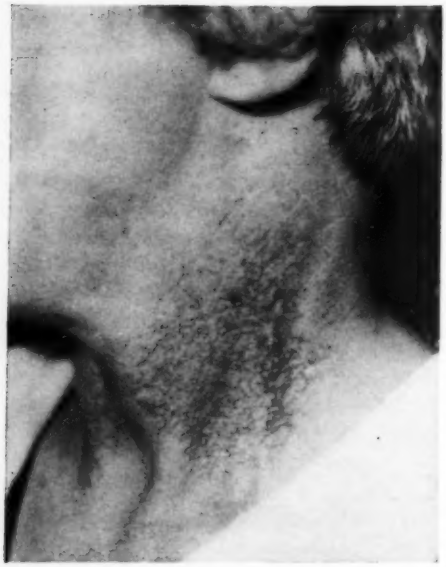

Fig. 7. Post-irradiation telangiectasis. This patient was treated for tuberculous lymph nodes in the left side of the neck, in 1922, receiving within seven months eight treatments at intervals of three to four weeks. Single doses of 8 Holzknecht units, *i.e.*, about 400 r, were given, the total dose thus amounting to about 3,200 r, with 0.5 mm. Zn filtration. Telangiectasis developed within the following year, as shown.

This same patient was treated again for a parotid tumor on the left side of the face in 1932. She received within three months 16 irradiations of 250 r each and 15 of 200 r each, a total of 7,000 r (filter as above). No telangiectases developed within the following three years. The doses were measured on the skin.

In conclusion, one may say that, while a similar degree of narrowing, if it is considerable (say 2 μ), may completely occlude a small arteriole but only incompletely occlude an accompanying venule, a narrowing of lesser degree (say 1 μ) may be overcome in the arteries but form an obstacle in the veins.

The differences in structure, mentioned above, between the arteries and the veins have an important bearing on their reaction to radiation. With a single application the dose required to produce telangiectasis amounts in larger fields to about twice as much and in smaller ones to about three times as much as is required to produce an erythema. The erythema preceding telangiectasis shows, as a rule, all three waves. Retrospectively, it may be added that a dose producing all three waves is likely to be followed eventually by telangiectasis. This is because the third erythema, as has been pointed out, is conditioned by a swelling of the endothelial cells of the veins. Even though the swelling regresses, the fluid which has passed the endothelium may induce proliferation of the fibrous tissue, and a narrowing of the venous lumen may result.

With repeated irradiation, experience has shown that, beside the amount of the total dose, that of the single doses also has a decisive influence on the development of telangiectasis. Two possibilities may be distinguished. In the first the single doses, although not necessarily productive of an erythema, are strong enough to produce an edema. They amount to about 400 r, measured on the skin, and are able to produce temporary epilation. In the second case the single doses are less than 400 r, insufficient to produce either edema or epilation. It has been our experience that when a dose of about 400 r is repeated, for example six times, totalling some 2,400 r, telangiectasis may be expected in the course of about a year. Remarkably enough, however, when the single doses are limited to 100, 200, or 300 r, no telangiectasis develops even after a total dose amounting to 4,800 r or more (Fig. 7). Furthermore, when doses of 400 r or more are used, telangiectasis develops regardless of whether treatment is given daily, weekly, or monthly, the reason being that an interval of about three months is necessary for the recovery of the vascular endothelium. When, however, subepilatory doses—100, 200, or 300 r—are used, no telangiectasis will develop even when irradiation is given daily. This is because such doses lie beneath the level required to produce an edema and a subsequent fibrosis in the veins.

Because they possess comparatively more fibrous and less muscle and elastic tissue, the veins are more easily compressible than the arteries, a factor contributing largely to the difference between the radiation ef-

fects on the two types of blood vessels. Under the influence of external pressure a stenotic effect may be produced more easily in a vein than in an artery and, since it is a narrowing of the veins which gives rise to telangiectasis, the conclusion suggests itself that this will develop more readily the more the veins are exposed to pressure from without. This is borne out in practice. Doses which by themselves are not sufficient to produce telangiectasis will bring about this effect when the irradiated area is exposed to pressure. Thus, in skin compressed by a truss, by a bone, by scars, or by subcutaneous fat (*e.g.*, in a pendulous abdomen) telangiectasis may develop even after comparatively small single and total doses. Similarly the atrophy and depigmentation of the skin resulting from the narrowing of the arteries are more pronounced where the vessels are subject to external pressure. In contrast to this, erythema and edema, resulting from dilatation of the capillaries, are more intensive in the absence of compression, *e.g.*, in areas containing much loose connective tissue, as the axilla or neck.

There is thus a contrast between the early and the delayed vascular phenomena following irradiation. While the early response, in the form of erythema and edema, referable to the capillaries, is less pronounced in regions exposed to external pressure, the later reactions—skin atrophy and telangiectasis, due to the narrowing of the arteries and veins respectively—are more severe in such areas.

The narrowing of the veins and arteries, though anatomically of similar nature, differs in significance with the two types of vessels. While the arteriofibrosis caused by the rays is of serious significance, the fibrosis in the veins is mainly of cosmetic importance, if any. Consequently a radiogenic atrophy of the skin represents a serious contraindication to further irradiation, but this does not apply to skin showing telangiectasis as the only alteration. Careful observations have shown that no further damage was produced in a telangiectatic area after irradiation with a dose amounting to half the dose which had produced the original lesion provided the skin showed no other visible changes, and that for the second treatment the single doses did not exceed 200 r measured on the skin. Under these conditions no further change was seen in the irradiated skin over a period of more than seven years.

THE LYMPH VESSELS

Little is known of the changes occurring in irradiated lymphatics, due largely to the difficulties encountered in their observation. Even the largest lymphatic vessels, such as the thoracic duct, are no wider than a small vein, and are thus not accessible to gross examination, while the lymphatic capillaries are inconspicuous even microscopically, since the lymph contains chiefly lymphocytes, with almost no red cells, and is therefore colorless. As a result, the lymphatics can be visualized only when they are filled with a dye such as silver nitrate, or particulate matter such as India ink. By this means valuable information regarding the anatomy and physiology of the lymphatics has been obtained.

The old theory, according to which the lymphatics develop from tissue spaces and grow by the addition of new tissue, has been abandoned and the lymphatic system is now recognized as "an outgrowth, a child of the blood vascular tissue" (Drinker and Field). Clark, Fedorowicz, and Sabin have shown that the lymphatics develop from the endothelium of the veins and grow by multiplication of the endothelial cells. In other words, "lymphatics are modified veins" (Sabin) and share with the veins many structural and functional properties. The jugular, abdominal, and iliac veins especially form offshoots from which the lymphatics develop, and it is the jugular vein into which the thoracic duct pours most of the lymph formed in the body. Thus the lymphatics form a side channel of the vascular ring.

Another new conception is that the lymphatic vessels are to be considered as forming anatomically a closed system and not a continuation of the tissue spaces, as was

previously thought. "If lymphatics open out into tissue spaces, every injection of a capillary plexus with a non-diffusible fluid should spread out into tissue spaces and obscure the vessel—which is most obviously not the case' (Sabin).

Thus, not the tissue spaces, that is, the clefts between the cells and fibers, but the capillaries constitute the last physiologically active units in the lymphatic system, as well as in the blood vascular system. While the lymphatic capillaries are composed of endothelium only, the larger vessels of the lymphatic system contain also muscle fibers and connective tissue and, as in the veins, valves as well.

The lymphatic capillaries form plexuses, exhibiting "a very constant topography in the different regions of the body, a constancy in position, number and particularly in direction for each region" (Gray). In the skin, "there is a superficial and a deep plexus of lymphatics. . . the one is in the corium and the other above the fatty tissue" (Hudack and McMaster), while the epidermis is deprived of lymph vessels, as it is of blood vessels.

The lymphatic capillaries are, as a rule, more deeply situated than the blood capillaries, and are far larger, measuring at least 15 μ in diameter as compared with 8 μ (0.008 mm.) for the blood capillaries. Their course is irregular, and they are alternately dilated and narrowed.

The walls of the lymphatic capillaries are composed of endothelial cells, slightly larger, thinner, and more rounded than the cells in the blood capillary wall (Maximow), resembling rather endothelial cells of the venules. As in the blood capillaries, the endothelial cells are normally permeable to water and salts, but impermeable to proteins and cells. "All of the evidence that we have obtained supports the view that the permeability of the lymphatic wall resembles the permeability of the capillary wall in its essential features and perhaps in its degree" (McMaster and Hudack). The permeability increases under the influence of various agents, as mechanical obstruction, mechanical stimulation, as by a stroke, heat, chemical irritants, and light. This applies, however, only to permeability for fluids and not particulate matter. It is a remarkable fact that the increase of permeability takes place without noticeable enlargement of the lymphatics.

Marked dilatation of the lymphatics is seen only when an edema in the tissue spaces is present, regardless of its origin. This was first shown by Clark in 1921, and subsequently generally corroborated. "This enlargement of the lymphatics," Clark says, "is characterized by a widening of the lumen, while the endothelial wall becomes thinner and smoother." The finding is striking because, "if the tissue fluid pressure rises, owing to the accumulation of fluid, the lymphatics should be compressed" (Pullinger and Florey). It is the more remarkable since, as Clark points out, the blood vessels are found to be narrower than normal in edema. Thus, the edema on one hand dilates the lymphatics and on the other compresses the blood vessels. An explanation for this peculiar fact was given by Pullinger and Florey, who found that, in contrast to the blood capillaries, the lymphatics are formed by an endothelium "to which fibers of the surrounding connective tissue are attached."

In the light of these findings, the mechanism of the dilatation of the lymphatic capillaries may be thought of as follows: When, for any reason, the permeability of the blood capillaries is increased, more fluid passes the wall and fills the perivascular neighborhood. A part fills the tissue spaces between the cells and fibers, forming the edema fluid. A part enters the structures and makes them swell. From the observations of Pullinger and Florey, it appears that "as the connective tissue fills with edema fluid and swells, tension on fibers attached to the lymphatic capillaries causes their walls to be drawn apart, their dilatation thus being passive."

If we recall that the blood capillaries dilate not because the endothelial cells are drawn apart from outside, but because they themselves are filled with fluid and conse-

quently increase in size, thus enlarging the lumen of the capillaries, the contrast between the two systems becomes obvious.

To this difference another may be added, still more important physiologically. While in the blood capillaries the fluid escapes at the arterial end and is resorbed at the venous end, no such difference exists between different parts of the lymphatic capillaries. These vessels may let the fluid pass from within and absorb the fluid from without at any point.

A further important difference between the two systems may be noted in observing an edema. It may be said that the edema is formed by the blood capillaries and resorbed by the lymph capillaries. In other words, in the blood capillaries production and in the lymph capillaries resorption prevails. This is demonstrated when an edema is produced artificially and a dye is then injected into the neighboring lymphatics. Under these circumstances there is no escape of the dye from the lymphatics but a continuous resorption of the edema from the tissue spaces. As a consequence, the dye is washed out and carried away, and transudation of the dye does not occur until the edema is resorbed.

The predominance of the resorptive force in the lymph capillaries is more easily understood if we consider first why resorption prevails at the venous end of the blood capillaries. This is known to be due to the fact that here the capillary pressure is lower, while the osmotic pressure is higher, than at the arterial end. The same relationship exists between the venous end of the blood capillary and the lymph capillary. In the lymph vessels the capillary pressure is low, since the action of the heart and the blood pressure exert no influence here. This is, incidentally, the reason why the lymphatic capillaries are readily compressed from without and consequently are seldom encountered in firm scar tissue. But while the capillary pressure is much lower, the osmotic pressure is much higher in the lymph than in the blood vessels. Best and Taylor explain this fact as follows: "The proportion of albumins to globulins is in the lymph higher than in the plasma, as a result of the freer passage of the former protein through the capillary wall."

As a result of these conditions, the resorption capacity displayed by the lymph capillaries is stronger than that of the blood capillaries. Consequently, while small quantities of fluid, such as are present in the stage of rest, are resorbed at the venous ends of the blood capillaries, increased quantities, formed during activity of the tissues and under pathologic conditions in the state of edema, are resorbed by means of the lymphatic system. With the fluid various salts, proteins, and other colloids leaving the blood capillaries enter the lymphatic capillaries. Finally, tissue débris, composed of dead or degenerated cells, and particulate matter artificially introduced, find their way into the lymphatics after phagocytosis by mononuclear or polynuclear cells endowed with the faculty of penetrating the endothelial walls of the lymph capillaries. This process is facilitated by the properties of the endothelial cells, mentioned previously: that is, they are thinner, larger, and more rounded than those in the blood capillaries. When these cells swell, the "stomata" between them become larger so that the leukocytes can more easily enter just as they emerged more easily from the structurally similar venules.

On the basis of the physio-anatomical facts presented above, we arrive at the following conclusions as to the radiation effects on the lymphatic vessels:

Influence on the Lumen: Since swelling of the irradiated cell is a universal phenomenon, it may be assumed to occur in the endothelial cells of the lymph capillaries. Rost was the first to mention specifically that, "as in the blood vessels, so too in the lymph capillaries, the endothelial cells are undoubtedly affected by the process of swelling." The consequences are the same as in the blood capillaries: Owing to the swelling in the frontal diameter the cells and the nuclei, respectively, will protrude into the lumen, producing a narrowing of the vessels. Since the lymphatic endo-

thelial cells are larger and rounder, the narrowing effect may be comparatively more pronounced than in the blood capillaries. It will naturally increase with the dose given to the vessels. This narrowing of the lumen of the lymphatics under the influence of radiation is seen clinically when, for example, after irradiation of a cancer of the larynx a more or less marked swelling of the submental region develops, ultimately to subside when the lumen of the irradiated lymphatics returns to normal. Narrowing of the lumen as a consequence of swelling of the endothelial cells of the lymphatics is also shown experimentally by Sugarbaker and Sugiura. These authors injected rats subcutaneously with diluted ink and irradiated the region twenty-four hours later. The regional lymph nodes examined two to four weeks afterward showed less pigment than was present in non-irradiated controls.

It may be assumed that the attachment of the endothelial cells to the connective tissue makes it impossible for them to swell in the transverse diameter. Consequently, *dilatation* of the lymph capillaries as a result of swelling of the endothelial cells cannot be brought about by irradiation. Irradiation can produce a dilatation in the lymphatics only by means of a perivascular edema. With the edema there is invariably associated a swelling of the fibrous tissue, leading to a dilatation of the lymph capillaries as described by Pullinger and Florey, quoted above.

When a dose is applied which is followed by a full-fledged three-wave erythema, then a dilatation of the lymph capillaries may also occur in three separate time periods, although not all three stages may be observed clinically. Two waves were observed in a case of cancer of the larynx treated by roentgen rays. The first swelling of the submental region subsided after a few days; subsequently, after a symptom-free interval of about three weeks a new swelling developed, this time lasting for many months (Fig. 8).

Influence on Function: A dye injected into the lymph vessels is observed to pass through the walls into the neighborhood. As has been mentioned, the permeability of the lymphatic walls can be increased by different agents, including heat and light. It is possible that roentgen and radium rays would produce a similar effect. Under physiological conditions, however, a permeation from within the lymph capillaries to the outside is of no particular importance, as these do not carry any substances needed by the tissues but, on the contrary, take away the final products of metabolic processes and the cell débris which cannot be transported by the veins. Accordingly there is no experience to support the conception that under normal conditions permeation of the lymphatics is increased under the influence of radiation. This is in accord with the fact that no dilatation occurs in the irradiated lymph vessels.

But in the same degree as permeation through the lymphatics from within is insignificant, so is resorption from without into the vessel lumen important. Here the true destiny of the lymphatic system becomes manifest. Here also the influence of radiation can be clearly proved. Ever since radiation therapy has been practised, it has been observed that under the influence of the rays resorption increases, in that acute, subacute, and chronic swellings and edemas frequently disappear. This, however, applies only to localized edema; in the generalized edema of cardiac or renal origin not the slightest effect can be seen.

Two groups of localized edema are to be distinguished. The first group comprises those cases due to obstruction of the lymph vessels. The obstruction may be caused by a tumor, and subside when radiation is able to destroy the growth, as in the case of metastatic lymph nodes in the axilla leading to swelling of the arm, sometimes to elephantiasic dimensions. Or the obstruction may be caused by a chronic inflammatory process, as in filariasis, which has proved completely curable by irradiation (Ross Golden and O'Connor), or other forms of "elephantiasis" (Sluys and others). The second group of localized edemas includes cases, usually of slight or moderate

Fig. 8. A. Post-irradiation edema, developing after completion of roentgen therapy, 3,500 r to each side of the neck, 0.5 mm. Cu filtration. Seven days after this picture was taken the edema had subsided to a considerable extent (B), but three weeks after this it recurred (C), persisting for months. There were no other post-irradiation changes in the skin.

degree, associated with an acute or subacute inflammation.

In such cases as have been described the blood capillaries dilate following irradiation, and their permeability increases. Subsequently the perivascular edema is enhanced, and finally the lymphatic vessels dilate. With dilatation of the lymphatics, caused primarily by a dilatation of the blood capillaries, the endothelial cells are held in tension and thinned while the intercellular "stomata" become enlarged. It is these changes which facilitate the resorption of the fluid accumulated in the perivascular tissues. In the measure that this is resorbed, the lymphatics become narrower and the fluid is set in motion, pushing forward the plug formed by thrombi and coagulated plasma which, according to Menkin, blockades the lymph vessels in inflammation.

As to the resorption of solid particles, such as cell débris or matter artificially introduced, one should recall that the irradiation of normal lymphatics causes a narrowing of their lumina, and subsequently makes the resorptive processes more difficult.

As to whether the resorption of tumor cells can be accelerated by irradiation, it may be said that the swelling of the endothelial cells—the more pronounced the higher the dose given—leads to a narrowing of the lumen, the best defense against the propagation of tumor cells. The narrowing effect in the lymph capillaries is reinforced by the changes taking place in the larger lymphatic vessels, consisting, like the arteries and veins, not only of endothelium, but also of a muscular and connective-tissue coat. These larger lymphatic vessels undergo post-irradiation changes similar to those described for the arteries and veins: subendothelial edema and finally fibrosis, narrowing the lumen and blockading transportation, especially as far as cells are concerned.

Radiosensitivity of Edematous Tissues: It has been pointed out that, while in edema accompanying an inflammatory process radiation leads to an increased resorption on the part of the lymphatics, no such effect is obtained in generalized edema. It may be added that the two conditions differ in still another respect. In comparison to the normal tissues, lower

doses are required to produce an erythema and other vascular phenomena in inflammatory edema, while higher doses are required for this purpose in the generalized condition. In other words, while in the state of inflammatory edema radiosensitivity of the tissues is increased, the contrary is true in non-inflammatory edema. The increased radiosensitivity of the inflamed tissues is due, quite obviously, to the underlying hyperemia, a factor well known for its influence on radiosensitivity of the tissues.

The fact that the tissues in the state of non-inflammatory edema exhibit a decreased degree of radiosensitivity, first noticed by Wintz in 1920, has been less understood. But the investigations of Clark throw light on the underlying mechanism. As has been mentioned before, Clark found that in generalized edema, while the lymphatics are markedly dilated, the blood vessels are narrowed, owing to compression by the edema. In other words, it is the anemia which renders the tissues less radiosensitive in the state of non-inflammatory edema, as it is the hyperemia which causes an increased radiosensitivity of the tissues in the inflammatory type.

Summarizing, it appears that normal lymphatic capillaries may be narrowed by larger doses while dilated lymphatic capillaries may be narrowed by smaller doses. No primary dilatation of the normal lymphatic capillaries appears to be obtainable by the action of rays. Tissues in the state of inflammatory edema are hyperemic and consequently of increased radiosensitivity, while tissues in the state of generalized edema are anemic and consequently of decreased radiosensitivity.

27 W. 86th St., New York, N. Y.

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CASE REPORTS

Meckel's Diverticulum[1]

ALFRED C. LEDOUX, M.D.
St. Francis Hospital, Evanston, Ill.

The numerous articles in current medical literature on the subject of Meckel's diverticulum mention radiologic examination as a diagnostic method, yet positive radiologic diagnosis appears infrequent.

The case presented below seems particularly interesting and worthy of report since the diagnosis was established by serial radiologic study of the small intestine, and subsequent surgical removal and pathologic study showed the lesion to be the cause of the signs and symptoms.

CASE REPORT

D. A., a white male, two and one-half years old, was referred for radiologic examination with the following history. Four days previously the child had complained of a feeling of weakness, which was accompanied by nausea and vomiting. The mother stated that the child "doubled up" with pain and looked "blue." The vomitus consisted of undigested food, which had been eaten some hours previously. Vomiting was followed in a short time by a copious watery bowel movement containing blood, both bright red and dark.

Physical examination was negative, and the past history was indefinite, although the mother stated that the child had on several occasions complained of vague abdominal pain to which she had attributed no significance.

Three days later the child was again seized with a sudden attack of pain not accompanied by vomiting. In the interim the stools had been black in color, but now bright red blood was again noted. Physical examination still remained negative, the only significant finding being a red cell count of 3,070,000 and a hemoglobin of 34.5 per cent. A bleeding polyp was regarded as being the most likely possibility, although duodenal ulcer was also considered.

Radiologic examination at this time included an anteroposterior view of the abdomen and examination of the colon with a barium enema, which revealed no positive evidence of any organic lesion. An attempt at air insufflation of the colon was unsatisfactory, due in part to the fact that it was deemed inadvisable, because of the bleeding, to cleanse the colon adequately.

Sigmoidoscopic examination was carried out on the following day, to a 20 cm. level. The mucosa appeared normal; no bleeding areas or polyps were seen.

Three days later x-ray examination of the gastro-intestinal tract with a barium meal was begun. The esophagus, stomach, and duodenal bulb, as well as the proximal coils of the small intestine, were normal. At the end of two hours the findings remained normal, but after four hours an extra-luminal shadow of barium, in the mid-line at the level of the sacral promontory (Fig. 1), could be demonstrated. This shadow was approximately 1 cm. in diameter and was movable. The region was tender to palpation. At the end of five hours the same shadow was demonstrable, and with the same findings as noted earlier (Fig. 2). On this combined evidence a radiologic diagnosis of a Meckel's diverticulum of the ileum was made.

Over a period of eighteen days symptomatic treatment was given, with transfusions of whole blood and plasma. At varying times during this interval there was evidence of further bleeding from the gastro-intestinal tract. Laparotomy was then performed. A diverticulum of the ileum was resected with a portion of the ileum, and a lateral anastomosis was made.

Examination of the specimen showed the diverticulum to be 12 mm. in diameter, lined distally with mucosa of the small intestine type, which was continuous with a thick layer of mucosa of gastric type. Near the base of the diverticulum the gastric mucosa was superficially necrotic for a distance of 7 mm. The pathologist's diagnosis was Meckel's diverticulum with gastric mucosa; peptic ulcer of the ileal margin of the diverticulum.

The postoperative course was uneventful, and the patient has remained symptom-free.

SUMMARY

A case is reported in which a radiologic diagnosis of Meckel's diverticulum was made, and subsequently confirmed at laparotomy.

The experience in this case would suggest that in patients with obscure gastro-intestinal bleeding, a more detailed study of the small intestine might increase the frequency of the preoperative diagnosis of this condition.

[1] Accepted for publication in February 1942.

355 Ridge Ave., Evanston, Ill.

Fig. 1. Meckel's diverticulum: film made four hours after the ingestion of the barium meal. The arrow points to the diverticulum.

Fig. 2. Meckel's diverticulum: film made five hours after the barium meal. The arrow points to the diverticulum.

Healed Gastric Ulcer with Associated Inflammatory Fibrotic Changes in a Diaphragmatic Hernia[1]

JOE C. RUDE, M.D.
Duke Hospital, Durham, N. C.

In reviewing the literature Bright (2), in 1836, recorded the first case of a gastric ulcer involving a diaphragmatic hernia with death from exhaustion after a long period of vomiting and dyspnea. Collier, Hurst, and Sheaf (3) in 1929 reported two more cases from Guy's Hospital, both in males. Mathews and MacFee (18) in 1931 reported fifteen cases of hernia in women from forty to fifty-eight years of age; all but one of this group were fairly obese, and such blood counts as were available showed anemias of varying degree. In two instances ulcers were present on the lesser curvature at the point where it was in contact with the constricting margin of the diaphragm. Few of the cases reviewed exhibited typical symptoms of ulcer, and for the most part the ulcer was unsuspected, being found either at operation or autopsy; some were even overlooked at operation.

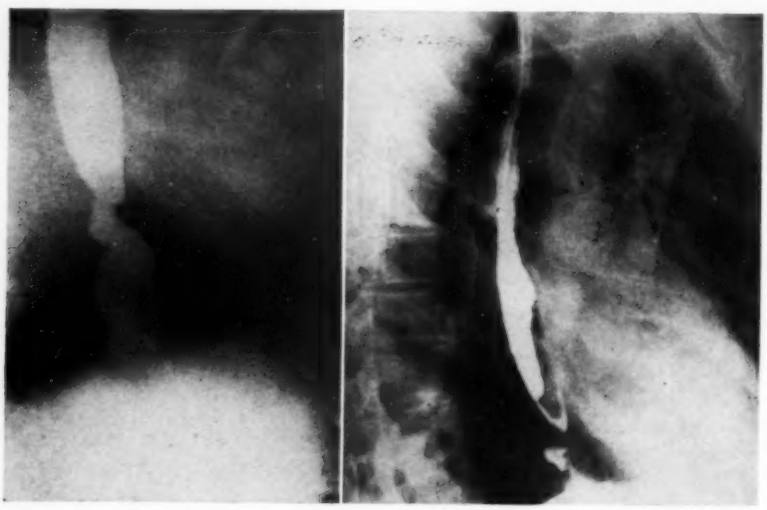
Diaphragmatic hernia ulcers are, as a rule, superficial erosions (9–10) that do not penetrate the stomach wall. The pressure exerted on the vascular supply by the margins of the hernial opening is a factor in the occurrence of these ulcer erosions (15–19). This constricting pressure produces congestion, varicosities, and disturbance of the arterial supply, followed in some instances by secondary infection and subsequent fibrosis of the surrounding stomach and esophageal wall. This latter finding was recorded by Morrison and Jones of Boston (19) and was suggested as a possible explanation for hematemesis or melena. Ulcers occur for the most part on the lesser curvature, a predisposing factor being stagnation of gastric contents, which are thus afforded an opportunity to act on the gastric mucosa.

The first evidence of the condition is mild epigastric distress most noticeable after a heavy meal and relieved by belching or vomiting. Attacks become more severe as more of the stomach becomes incorporated in the hernia, with pain radiating to the back, usually to the left of the spine. Pain may become agonizing on account of spasm of the diaphragm and reflex cardiospasm. It may even

[1] Accepted for publication in February 1942.

simulate a cardiac condition (12). In the later stages weakness and shortness of breath are prominent symptoms.

Key (16) reports a case of gastric ulcer in a diaphragmatic hernia cured by operation, and Nord (20) reports one successfully treated by phrenic neurectomy. In the case to be reported here an ulcer was suspected on fluoroscopic examination, and a healed gastric ulcer site was verified postmortem, microscopic sections showing resultant damage in the way of fibrosis and thickening of the tissues and muscular structures of the diaphragmatic portion of the stomach and adjacent esophagus.



Figs. 1 and 2. Case 1 (J. C.): Figure 1 (left) shows the lower end of the congenitally short esophagus and the amount of the stomach above the diaphragm. Some idea is also gained of the degree of constriction due to fibrosis at the lower end of the esophagus. Figure 2 (right) shows the niche in the supradiaphragmatic portion of the stomach, immediately below the lower end of the esophagus.

CASE REPORT

J. C., a 62-year-old white man, was admitted July 20, 1937, with a two-year history of difficulty in swallowing, first of solid foods and within the past month even of liquids. Regurgitation was a prominent symptom. A laryngeal biopsy had shown chronic inflammatory tissue, and an esophagoscopy was non-contributory. Gastro-intestinal studies showed a diaphragmatic hernia of the short esophageal type in which an ulcer was suspected, but not diagnosed because barium failed to stay in the niche.

On physical examination the patient appeared chronically ill, dehydrated, and extremely emaciated, with severe arthritic changes in the hands, fingers, toes, and knees. Mucous membranes of the oral cavity and tongue were smooth and red. The chest and abdominal findings were essentially negative, except for a soft systolic heart murmur. The prostate was several times the normal size.

The urine on admission showed an occasional granular cast and a trace of albumin. Stool examination on one occasion was benzidine-positive for blood.

Parenteral fluids and blood transfusions prepared the patient for operation, but it proved impossible to ascertain the nature of the lesion in the diaphragmatic hernia. Pharyngeal edema occurred after operation and adrenalin and throat suction did not relieve the condition, though oxygen furnished some relief. Recurring dyspnea was apparently aggravated by transfusions and infusions. On the third postoperative day audible râles developed in both lungs. Death occurred on the fourth day.

Necropsy disclosed chronic inflammation of the esophagus near the cardia with fibrosis and stenosis, and a congenital anomaly with insertion of the diaphragm at the cardiac antrum. In the diaphragmatic hernia of the short esophageal type a stellate scar was present which, according to a recent review (25), definitely establishes this in the supradiaphragmatic portion of the stomach. Multiple hemorrhagic and ulcerated areas were present on the posterior wall. Other findings were a gastrostomy wound, atelectasis (partial) of the right lower and

middle lobes of the lung with early pneumonia, and arteriosclerosis involving the coronary arteries, aorta, and common iliacs.

Microscopic sections showed gastric mucosa above the diaphragm and a depressed scar in the gastric mucosa just below the thickened, fibrotic, and stenosed lower end of the esophagus. The mucosa and circular and longitudinal layers of the muscularis externa of the esophagus were greatly thickened, infiltrated with small lymphocytes and plasma cells, and fibrosed.

Three years elapsed before another case of this nature was observed, but the patient is still living and a follow-up has proved unsatisfactory. Briefly the chief findings in this second case were epigastric distress over a number of years, gradually becoming more severe. Finally evidence of gastro-intestinal hemorrhage appeared: dizziness weakness, fainting, and the passage of tarry stools. The red blood count was two million, with hemoglobin 38 per cent. A niche was demonstrable fluoroscopically and films showed a diaphragmatic hernia of the short esophageal type. Barium was still present in this area at the end of six hours and this was considered presumptive evidence of either ulceration or erosion.

DISCUSSION

The condition discussed is not a common one, but occurs more frequently than is at present recognized. It appears to be more common beyond middle age, but occurs also in younger persons, both males and females. The incidence may be slightly greater in obese women (18).

Both of the patients referred to above showed a rather severe anemia, weakness, anorexia, and epigastric discomfort best relieved by milk and cream. Epigastric distress became gradually worse over a period of two years in the first case and progressed for twenty years in the second. Finally ulceration appeared with signs of anemia, and phenomena resulting from secondary infection in the walls of the herniated portion of the stomach and lower end of the esophagus manifested themselves. A point well worth remembering is that bleeding can and does occur from diaphragmatic hernias with or with-

Figs. 3 and 4. Case 2: Gastric ulcer in diaphragmatic hernia. Note wafer like area of increased density immediately above the diaphragm in Fig. 3 (left). Figure 4 (right), a six-hour film, shows retention of barium on what is assumed to be an eroded or ulcerated surface in the supradiaphragmatic portion of the stomach. The patient had taken nothing by mouth since the barium meal six hours before.

out the presence of ulceration, and this makes the evaluation of a diaphragmatic hernia all the more important and difficult.

These lesions are best demonstrated with the patient in the recumbent and Trendelenburg position with the body turned to the left side.

For those who are interested in the anatomy, etiology, classification, and pathological conditions in diaphragmatic hernias the following bibliography is suggested.

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EDITORIAL

Howard P. Doub, M.D., Editor

John D. Camp, M.D., Associate Editor

Aseptic Necrosis of Bone

The roentgen signs of bone necrosis and of the presence of devitalized bone of unknown origin have long been familiar, but it is only within the last few years that these have been correlated with the mechanism responsible for their production. Many of these lesions have been shown to be the end-result of an interruption of circulation, with the formation of bone infarcts.

In a recent series of articles Phemister (1) calls attention to the bone changes consequent upon interruption of the circulation, whether as a result of injury or disease, and reviews the studies leading to our present knowledge. The first information on the subject, he says, was obtained from a study of transplanted bone. It was originally thought that the entire transplant remained alive but Barth demonstrated that the transplanted bone dies and later is invaded and replaced by new bone. That the periosteum and endosteum of the transplant survive and take the most active part in generating the new bone was demonstrated by Axhausen. The same process occurs in fractures, where there is necrosis of the cortex adjacent to the fracture with subsequent creeping replacement by new bone.

Instances of aseptic necrosis in other than transplanted bone have long been recognized in the epiphyses and short bones both in children and adults, in such conditions as Legg-Perthes disease, Osgood-Schlatter disease, Köhler's disease of the tarsal navicular, and Kienböck's disease of the semilunar bone. Phemister states that new bone almost completely replaces the aseptic necrotic bone in Legg-Perthes disease and that the process proceeds more rapidly in these young patients than in adults. In necrosing lesions of the epiphyses the cartilage may show evidence of nutritional disturbance in places but in large part it remains alive, becomes thicker than normal, as in Legg-Perthes disease, and after the necrotic bone is replaced takes part in further epiphyseal growth.

Roentgenology has inevitably played a large part in the study of the skeletal changes resulting from circulatory blockage, making it possible to observe in the living those changes which have been seen in pathologic specimens. No demonstrable changes are present in the early stages of necrosis but in time atrophy of disuse of the surrounding bone can usually be demonstrated while the dead bone retains its normal density. As regeneration occurs, particularly if there has been serious interference with function, the new bone is less dense than the old which it replaces, and casts a fainter shadow.

One of the most common examples of devitalized bone resulting from loss of blood supply is seen in the head of the femur following fractures through the femoral neck. In some instances this results in non-union or poor union of the fragments. Union is more apt to ensue after accurate replacement and fixation by surgical means. According to Phemister, it occurs by the formation of fibrous callus in the cancellous spaces of the distal end of the neck, extending across the fracture into the head. There is no periosteal callus and the fibrous callus is transformed directly into bone. Connective tissue then invades the head and is gradually transformed by metaplasia into new bone. This may occur very

slowly, the process continuing for months or years until all dead bone is replaced or enclosed. Such transformation may go unrecognized except in cases of collapse of the untransformed portion of the head due to premature weight-bearing or the development of chronic arthritic changes. In instances of non-union the entire bony head usually becomes necrotic, while osteoporosis occurs in the adjacent bone as a result of disuse, so that the devitalized head appears much more dense on the roentgenogram. The process of revascularization and fibrous tissue infiltration of the marrow spaces is much slower in these cases and usually requires apposition and fixation of the fragments. Areas of local change around the hip are often present.

Traumatic dislocation may be followed by interruption of the circulation with changes in the bone similar to those which are found after fracture. These changes are occasionally the sequelae of dislocation of the hip. Banks (2) recently reported a number of such cases and reviewed the literature. Another dislocation with loss of blood supply but without associated fracture is that of the carpal lunatum. In dislocation of this bone the dorsal attachments are torn and, since its blood supply is derived mainly from this source, devitalization and necrosis may follow. If the dislocation is unreduced, dissolution and replacement by bone of lesser density usually occur.

Bone infarcts may also occur in nontraumatic conditions, as pointed out by Phemister in the second of his papers. The most familiar example of this nontraumatic type is furnished by caisson disease, observed in workers in compressed-air chambers. In Phemister's cases, infarcts, some in the shafts and some in the epiphyses of the long bones, were visible in the roentgenograms. They were indicated by areas of necrosis with irregularly calcified walls and sometimes by collapse and sequestration as a result of weight-bearing. When the epiphysis is involved adjacent to the articular surface, the overlying cartilage undergoes either extensive or complete necrosis. In such cases chronic deforming arthritis may be a late sequela. If the necrotic area occurs in the shaft, small infarcts may be replaced by new bone but large ones become walled off by fibrous tissue, which eventually ossifies, with the formation of a sharp line of demarcation.

On another page in this issue of RADIOLOGY Bell, Edson, and Hornick (3) describe in detail the theories which have been advanced to account for the bone changes in caisson disease. The gas embolism theory, according to which nitrogen is absorbed by the tissues in excess amount, forming bubbles upon too rapid decompression, is now generally accepted. Bell and his associates carried out x-ray studies on 32 caisson workers who presented no clinical symptoms. They discovered positive bone or joint changes in 75 per cent of all those examined. The changes appeared to bear a direct relation to the duration of employment and its consecutiveness.

Phemister believes that bone infarction may also be associated with arteriosclerosis and advocates the routine roentgen and pathologic examination of all bones of extremities amputated because of arteriosclerotic gangrene. He also discusses the relationship between bone infarcts and chronic hypertrophic arthritis and presents case reports which suggest a relationship between the two.

The subject of aseptic necrosis of bone is a fascinating one and is becoming better understood because of the interest recently awakened by such studies as the one here cited. It is only within the past few years that reference to the condition has been found at all in the medical literature. As more detailed information is acquired, it is quite probable that other chronic bone diseases will be found to be related to interruption of the blood supply.

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ANNOUNCEMENTS

CANCER TEACHING DAY

Buffalo, N. Y.

Cancer Teaching Day will be observed on Thursday, June 18, beginning at 2:00 P.M., at the Hotel Statler, Buffalo, under the auspices of the Erie County Medical Society, the University of Buffalo School of Medicine, the Eighth District Branch of the New York State Medical Society, the Medical Society of the State of New York, and the New York State Department of Health, Division of Cancer Control.

The following program has been arranged:

Cancer of the Larynx: Early Diagnosis and Criteria for the Selection of Methods of Treatment (illustrated by motion pictures and lantern slides), CHEVALIER L. JACKSON, M.D., Professor Clinical Bronchoscopy and Esophagoscopy, School of Medicine, Temple University, Philadelphia, Penna.

Hematuria and Cancer of the Genito-Urinary Tract, GEORGE F. CAHILL, M.D., Professor of Urology, College of Physicians and Surgeons, Columbia University, New York.

Carcinoma of the Breast: Diagnosis, Treatment, and Results, Frank E. Adair, M.D., Executive Officer, Memorial Hospital, New York.

Surgery and Radiation in the Treatment of Malignancies of the Colon and Rectum, THOMAS E. JONES, M.D., Surgeon, Cleveland Clinic, Cleveland, Ohio.

Dinner: 6:30 P.M.

Recent Studies in the Production of Cancer by Chemical Compounds; the Conditioned Deficiency as a Mechanism, CORNELIUS P. RHOADS, M.D., Director, Memorial Hospital, New York.

CHICAGO ROENTGEN SOCIETY

At the meeting of the Chicago Roentgen Society, April 9, 1942, the following officers were elected: Chester J. Challenger, M.D., President; Earl E. Barth, M.D., Vice-President; Warren W. Furey, M.D., Secretary.

RADIOLOGICAL SOCIETY OF NEW JERSEY

At the Annual Meeting of the Radiological Society of New Jersey, held in Atlantic City on April 22, 1942, the following officers were elected: President, W. J. Marquis, M.D., Newark; Vice-President, H. A. Vogel, M.D., Elizabeth; Secretary, H. J. Perlberg, M.D., Jersey City; Treasurer, C. Oderr, M.D., Westfield; Counsellor, C. A. Plume, M.D., Succasunna.

OHIO STATE RADIOLOGICAL SOCIETY

The annual meeting of the Ohio State Radiological Society was held in Columbus, Ohio, April 30, 1942, and was attended by members from all the cities of Ohio. The guests were Dr. John H. Lawrence of Berkeley, Calif., and Dr. M. C. Sosman of Boston, Mass. The officers elected for the ensuing year were: U. V. Portmann, M.D., Cleveland, President; E. C. Baker, M.D., Youngstown, Vice-President; and J. E. McCarthy, M.D., Cincinnati, Secretary and Treasurer.

TENNESSEE RADIOLOGICAL SOCIETY

The annual meeting of the Tennessee Radiological Society was held in Memphis, Tennessee, April 15. The guest speaker was Dr. Robert J. Reeves of Duke University, Durham, N. C. The officers for the ensuing year are: Horace D. Gray, M.D., Memphis, President; Franklin B. Bogart, M.D., Chattanooga, Vice-President; J. Marsh Frère, M.D., Chattanooga, Secretary-Treasurer.

In Memoriam

HARRY B. MAGEE, M.D.

1884–1942

Dr. Harry B. Magee, of Peoria, Ill., died at his home on April 20, 1942. Dr. Magee was born in Clarion, Penna.; he was graduated in 1908 from the University of Pennsylvania and since 1910 had practised in Peoria. He was a member of the Radiological Society of North America, of the Illinois Roentgen Society, of which he was Past President, and of local medical organizations. He was also Past President of the Section of Radiology of the State Medical Society and of the Staff of the John C. Proctor Hospital, Peoria.

Radiological Services During the War

With estimates of the prospective needs for physicians in the military forces ranging as high as 50,000, it is obvious that the depletion of those engaged in civilian practice will be severe. All indications point to a particular shortage of radiologists. There are approximately 2,800 radiologists of all degrees of competence in the United States, about 50 per cent of whom are under forty-five years of age. Of the total classified as radiologists, approximately 1,500 have been certified by the American Board of Radiology. These figures give an approximation of the supply of radiologists available for both the armed forces and the requirements of the civilian population. To meet the requirements of the Army and Navy, what will be the demand?

MILITARY DEMANDS

The Committee on Military Affairs of the American College of Radiology (the members of which compose also the Subcommittee on Radiology of the National Research Council) has for several months past been in frequent conference with representatives of the Surgeons General and the Procurement and Assignment Service. The most recent information obtained by the Committee indicates that there will be about 51,750 physicians under forty-five available for the armed forces after deducting the physically unfit, those retired, females, Negroes, aliens, and unlicensed graduates. For an Army of 10 million men, 65,000 physicians will be needed. An estimated 4,200 will be required by the Navy.

On Feb. 13, 1942, the Committee was advised that there were 163 radiologists in the Medical Corps as of that date. It was estimated that an additional 1,000 would be needed by the end of 1942 to fulfill the requirements of an Army of 3,600,000 men. The immediate demand for nearly 600 trained radiologists in the Army Medical Corps on the above date has since been fulfilled, and the Committee was recently advised that there is at present no unfilled demand. Two sources have supplied radiologists to bring the personnel up to the desired number: radiologists in the Organized Reserve, and regular officers of the Medical Corps who have completed short courses of basic roentgenological training in the Army Medical School.

The Committee on Military Affairs has recommended an expanded program to increase the number receiving basic training. The Army Medical School is presently turning out about 25 medical officers each month after completion of a four-week basic course which prepares them to act as assistants to specialists in roentgenology. Another source of additional personnel will be supplied by the more than 100 men who will complete three-year residencies this year and, presumably, each year thereafter. The requirements of the Navy are relatively small and are at present filled.

With this brief picture of the probable demands and the available supply of radiologists for the armed forces, it is apparent that there will not be a sufficient number of radiologists left in civilian practice to fulfill the medical needs of the civilian population with the same adequacy as before. Although the health needs of the civilian population are likely to increase rather than decrease, it is obvious that the demands of the armed forces will be filled first and civilian needs will be met as best they can with the physicians left in private practice.

A PLAN FOR MAINTAINING RADIOLOGICAL SERVICE DURING THE WAR

The radiologist who leaves a lucrative private practice and enters the service of his country is making a real sacrifice. In order that the best service possible under the circumstances may be maintained for the civilian population, those carrying on at home must also make sacrifices. A mutual and patriotic spirit must prevail among patients, hospital staffs, referring physicians, and radiologists remaining in private practice.

By authority of the Board of Chancellors of the American College of Radiology, the Executive Committee of the Board has prepared a plan, consisting of general principles, that is recommended for the consideration of community hospitals and regional radiological societies in adopting a course of procedure to meet the situation created by the emergency.

The plan has a three-fold objective: (1) to encourage radiologists of military age to volunteer for commissions in the armed forces; (2) to maintain the highest quality of radiological service for the civilian population that is possible under the circumstances; (3) to protect the interests of physicians in the armed forces during the period of their service.

The problems and the recommended solution will vary according to different situations and in each community. The procedure to be followed will depend upon the nature of the practice involved, the size of the community, and the number of qualified radiologists remaining in the community.

The Private Office

If a radiologist entering military service has a private office, he may engage a locum tenens to care for his practice during his absence. If a physician can be obtained to carry on the practice on a full-time or part-time basis, a simple solution is pro-

vided. A private contract can be entered into according to the agreement of the parties. If the absentee has a hospital practice in addition to his office practice, the agreement will usually cover both. In the latter event, the approval of the hospital staff and its administrators should be obtained for the locum tenens to substitute on the staff for the absentee. Further details of the agreement with the hospital are discussed below.

Where a locum tenens is engaged, his compensation is a matter for private negotiation. It is thought that in the usual instance, 75 per cent of the net income from the practice, both in the office and hospital, would be a fair compensation and allow an adequate sum to the absentee. (A sample contract for a locum tenens can be obtained from the American College of Radiology.)

Manifestly, increasing depletion of the civilian ranks will make it difficult, if not impossible, to obtain one person to substitute for the absentee. This will call for a mutual pledge of co-operation on the part of all radiologists in the community. Two or more local radiologists may agree to divide the work, in which case their share of the net income would be divided according to the amount of time contributed by each.

The Hospital

It should be borne in mind that the interests of the hospital must be given full consideration in any plan adopted by a regional radiological society for maintaining the practice of its members serving with the armed forces. While it is under a moral obligation to co-operate in a plan of such altruism, the hospital is under no legal duty to accept a substitute of another's choosing or to continue its contract with the absentee radiologist. Instances, however, will undoubtedly be rare in which the hospitals of a community fail to co-operate in attaining the objectives sought in the proposed program.

The problems involved in hospital practices will vary according to the nature and size of the institution, as well as the size of the community. They may be classified as follows:

(1) *Full-Time Teaching Positions in Large Institutions:* Usually the director of a department will be classified as essential for teaching and will not be called to military service. In the event that he is called, he will probably have a teaching staff capable of carrying on in his absence. Otherwise, the situation may be met in the same manner as for other hospitals, as outlined below.

(2) *Full-Time Positions in Private Hospitals:* Three possible solutions are presented:

(*a*) A locum tenens may be obtained and, with the approval of the hospital staff and administrators, a private agreement may be executed between the parties. Since the volume of work in such a department is commonly due in considerable degree to the efforts of the director, it would seem that a reasonable compensation to the locum tenens would be somewhere around 75 per cent of the net return, the remainder going to the absentee.

(*b*) Radiologists remaining in the community may agree to look after the hospital practice of their absent colleague, and two or more may share in the conduct of the department. The approval of the institution would of course be necessary. The division of the income paid to the professional staff, between those performing the work and the absentee, should be agreed upon between the parties with the advice and recommendations of the hospital and the local radiological society.

(*c*) The hospital may obtain another radiologist to take over the department. As stated before, the hospital should, out of fairness, permit the physician entering service to select his own substitute, subject to its approval. The appointment of the substitute should be temporary, and the absentee should be guaranteed his place on the staff when he returns.

(3) *Part-Time Positions in Private Hospitals:* The practical and perhaps the ideal solution for this problem will be for one or more local radiologists to care for the work during the absence of the man in service. Provided the income of the department is maintained at its previous level, there appears no reason why the hospital should not agree to continue its existing financial arrangement and pay the same percentage or salary to substitutes as was paid before. A portion of the net income of the practice would normally be sent to the absentee or his family.

Small Cities: In some communities there will be only one radiologist conducting both a private office and one or more hospital departments. Usually the hospital department will not be large enough to warrant the engagement of another radiologist (even if such were available), and in this case the staff should be encouraged to be content with such service as a technical staff may provide. While this is far from a desirable solution, it will in many instances be the only one possible. Wherever possible a qualified radiologist from a neighboring community should be obtained to act as a consultant and visit the department at regular intervals.

Agreement among Radiologists

In setting out to draw up a plan for attaining the objectives which are outlined in the beginning of this discussion, the local radiological society or group of radiologists should first arrive at a common understanding and enter into a mutual agreement of co-operation. Though it may not be strictly necessary, it will usually be best to reduce the agreement to writing and ask each member to subscribe to it. A few basic principles to be incorporated in the agreement may be suggested as follows:

(1) Those radiologists remaining at home shall agree to make a patriotic contribution in time and effort in the interests of any of their colleagues entering the service of their country. In doing so they will have made the first and most important contribution toward accomplishing the three ob-

jectives of the program. They will have encouraged their colleagues of military age to volunteer for military duty; they will have assured the best radiological service to the community that is possible under the circumstances; and they will have protected the interests of their absent colleague.

(2) Any member entering service should be free to enter into a private contract with a locum tenens or an individual radiologist in the community on any basis he desires. If, however, he needs the assistance of the local society or group, he should know that his practice will be looked after and the work will be shared by those staying at home.

(3) A committee of three or more should be appointed to serve for the duration as advisors and mediators under the plan. It may be wise to ask an officer of the local county medical society to serve on the committee. This committee would be charged with the responsibility of determining the amount of time each radiologist could devote as a substitute in another office or hospital. It would offer advice to members entering service and make suggestions to the local profession regarding its work and endeavor to enroll the co-operation of referring physicians.

The committee should confer with the state chairman on Procurement and Assignment with a view toward obtaining deferment of radiologists who are essential for industrial and civilian practice. A sufficient number should be classified as essential to provide at least a minimum of radiological service in the community. It may become the responsibility of the committee to designate those individuals to be thus classified.

(4) A reasonable portion of the net income of the practice, over expenses, should be reserved for the absentee. In some communities the radiologists have already agreed that they will look after the practice of any colleague in the service and send him the entire net income after actual expenses are deducted. Normally, a fair portion of the net income will be divided among those performing the work.

(5) In the case of a private office, the entire local profession should be advised that the practice will be continued and an appeal should be made for physicians who have referred work to the absentee to continue to send it to his office. The technical and clerical staff should be kept intact and all bills should be rendered on the billhead of the absentee. Reports should be signed by the substitute "for Dr. Blank," the absentee.

(6) In the case of hospital practices the same general plan would be followed, but it would, of course, be necessary to reach an agreement with the hospital and obtain its approval for substituted service by one or more local radiologists. A meeting between the appointed committee and hospital representatives should be arranged for the purpose of securing the approval and support of hospitals in the plan.

Agreement among Hospitals

In connection with the maintenance of hospital service, a plan recently adopted by the Chicago Roentgen Society is of interest. A committee of three was appointed which sent a questionnaire to every member of the society to determine what hours each could devote in providing service in a hospital temporarily without a radiologist. The members were also asked to indicate the areas of the city they could most conveniently serve. Although any member was free to enter into a private contract with a locum tenens, the society officially stated its policy that, after reasonable expenses and any losses from his own practice were deducted, a substitute should pay over the net income from the hospital practice to the absentee. It is anticipated that in some instances several radiologists will be required to alternate in a department which has had a full-time director. The plan is at present functioning with apparent success.

Co-operation of the local hospitals is essential if the problems created by the emergency are to be solved with success. A program in the nature of the one here described is manifestly completely altruistic and patriotic in its motives and it seems unlikely that any hospital would offer objections. However, the hospitals must agree to accept substitutes and they must be content to get along with less complete service than that to which they are accustomed. The hospital administrators, medical staffs, and patients must realize that less than ideal conditions will prevail as a result of the emergency. They will be called on to share in the sacrifice made by the radiologist entering service and his colleagues who agree to render the service in his absence.

It will be necessary for those hospitals fortunate enough to retain their radiologist to consent to his contributing a portion of his time in other hospitals when called upon to do so for the welfare of the community at large. All these problems should be discussed in a conference with representatives of the hospitals in the early stages of the proposal. In all probability there will be an acute shortage of radiologists in civilian practice and it should be clearly understood by hospitals that temporary adjustments must be made. They will find it increasingly difficult to obtain a new radiologist for full-time or even part-time service. The practical solution provided in a proposal of this type should receive their complete co-operation.

Different problems will be presented according to the type of financial arrangement existing between a hospital and a radiologist whose work is to be carried on by substitutes. They may be briefly discussed under the following classifications:

Rental Arrangements: Where the radiologist pays a fixed rental or a rental based upon a percentage of the gross receipts of the department, his legal status is that of a tenant. He is not an employee or agent and normally will be free to sublet to one or more

radiologists, presuming they are acceptable to the staff and the administrators. In such cases the rental would remain the same and the division of the net income of the department would be a matter for negotiation with the substitutes.

Percentage Arrangements: Some contracts are of such a nature as to make the radiologist an employee of the hospital on a commission basis. As stated before, the hospital is under no legal duty to accept a substitute or to continue the contract under existing terms. Usually, however, it seems certain that the hospital will recognize its moral duty to participate in a program advanced for the welfare of the community, and will consent to a substitute acceptable to the staff. In most instances the same percentage would be paid to the substitute as was paid to the absentee and the division of this sum would be left to these parties. Where the volume of work or the receipts of the department are materially decreased by reason of less time from the temporary director, it might become necessary to reduce the percentage to the director to offset increased expenses incurred by the hospital.

Salary Arrangements: Where the director of the department is employed on a salary, the compensation to the substitutes would depend upon the amount of time they were able to give to the department in relation to that formerly given by the radiologist whose place they are filling. If the same amount of time were rendered, the salary would usually remain the same and would be divided among the substitutes according to the period each devoted. They in turn would divide on an agreed basis with the absentee. The advice of the committee of the radiological society should be helpful in reaching an agreement on these matters.

SUMMARY

The essential principles of the plan here proposed may be summarized as follows:

1. It is obvious that demands of the armed forces will create an acute shortage of radiologists available for the health needs of the civilian population.

2. To solve the problems created by the emergency, the American College of Radiology proposes the adoption of a plan having a three-fold objective: (*a*) to encourage radiologists of military age to volunteer for commissions in the armed forces; (*b*) to maintain the highest quality of radiological service for the civilian population that is possible under the circumstances; and (*c*) to protect the interests of physicians in the armed forces during the period of their service.

3. The plan calls for a spirit of co-operation among radiologists, hospitals, and referring physicians in the community.

4. A special committee of radiologists, with perhaps a member representing the county medical society, should be appointed to work out the program best suited to the community. The members of the Committee would act as advisors and mediators under the plan. The committee should confer with the state chairman of Procurement and Assignment concerning the deferment of radiologists essential for civilian practice.

5. A meeting should be held with hospital representatives to secure the approval and co-operation of the hospitals according to a specific plan of procedure.

6. Where one or more radiologists substitute in the private office of a man entering military service, referring physicians should be publicly urged to continue to send their patients to the office. Bills should be sent and reports signed in the name of the absentee. An agreed portion of the net income should be reserved for the absentee.

7. The arrangement in hospitals will vary depending upon whether the position is full or part time, and according to the existing fiscal arrangement between the radiologist and the hospital. Inasmuch as a new radiologist will in all probability not be available, local men remaining at home will usually be called upon to share in the work.

8. Members of the local radiological society should be asked to pledge their co-operation and subscribe to a specific set of principles.

9. Hospitals should grant leaves of absence to radiologists entering the service of their country and should agree to accept one or more substitutes to carry on the work, provided these are acceptable to the staff and the institution. Those hospitals which retain their radiologist should consent to his devoting a portion of his normal time to other departments, if called upon to do so.

MAC F. CAHAL

RADIOLOGICAL SOCIETIES OF NORTH AMERICA

Editor's Note.—Will secretaries of societies please cooperate by sending information to Howard P. Doub, M.D., Editor, Henry Ford Hospital, Detroit, Mich.

UNITED STATES

Radiological Society of North America.—Secretary, D. S. Childs, M.D., 607 Medical Arts Building, Syracuse, N. Y.

American Roentgen Ray Society.—Secretary, Harold Dabney Kerr, M.D., Iowa City, Iowa.

American College of Radiology.—Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill.

Section on Radiology, American Medical Association.—Secretary, J. T. Murphy, M.D., 421 Michigan St., Toledo, Ohio.

ARKANSAS

Arkansas Radiological Society.—Secretary-Treasurer, J. S. Wilson, M.D., Monticello. Meets every three months and annually at meeting of State Medical Society.

CALIFORNIA

California Medical Association, Section on Radiology.—Secretary, Joseph D. Coate, M.D., 434 Thirtieth St., Oakland.

Los Angeles County Medical Association, Radiological Section.—Secretary, Donald R. Laing, M.D., 65 N. Madison Ave., Pasadena. Meets second Wednesday of each month at County Society Building.

Pacific Roentgen Society.—Secretary-Treasurer, L. Henry Garland, M.D., 450 Sutter St., San Francisco. Society meets annually during annual meeting of the California Medical Association.

San Francisco Radiological Society.—Secretary, Earl R. Miller, M.D., University of California Hospital. Meets monthly on third Thursday at 7:45 P.M., for the first six months at Toland Hall (University of California Medical School); second six months at Lane Hall (Stanford University School of Medicine).

COLORADO

Denver Radiological Club.—Secretary, Edward J. Meister, M.D., 366 Metropolitan Bldg. Meetings third Friday of each month at the Denver Athletic Club.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Secretary-Treasurer, Max Climan, M.D., 242 Trumbull St., Hartford. Meetings bimonthly, on second Thursday. Place of meeting selected by Secretary.

FLORIDA

Florida Radiological Society.—Secretary-Treasurer, Walter A. Weed, M.D., 204 Exchange Building, Orlando.

GEORGIA

Georgia Radiological Society.—Secretary-Treasurer, Robert C. Pendergrass, M.D., Prather Clinic Bldg., Americus. Meetings twice annually, in November and at the annual meeting of State Medical Association.

ILLINOIS

Chicago Roentgen Society.—Secretary, Warren W. Furey, M.D., 6844 S. Oglesby Ave. Meets at the Palmer House, second Thursday of October, November, January, February, March, and April.

Illinois Radiological Society.—Secretary-Treasurer, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly by announcement.

Illinois State Medical Society, Section on Radiology.—Secretary, Earl E. Barth, M.D., 303 E. Chicago Ave., Chicago.

INDIANA

The Indiana Roentgen Society.—Secretary-Treasurer, Harold C. Ochsner, M.D., Methodist Hospital, Indianapolis. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

KENTUCKY

Kentucky Radiological Society.—Secretary-Treasurer, Joseph C. Bell, M.D., 402 Heyburn Bldg., Louisville. Meeting annually in Louisville, third Sunday afternoon in April.

LOUISIANA

Louisiana Radiological Society.—Secretary-Treasurer, Johnson R. Anderson, M.D., North Louisiana Sanitarium, Shreveport. Meets annually at same time as State Medical Society.

Shreveport Radiological Club.—Secretary-Treasurer, W. R. Harwell, M.D. Meetings monthly on the second Wednesday, at the offices of the various members.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Secretary, Walter L. Kilby, M.D., 101 W. Read St. Meetings are held the third Tuesday of each month.

MICHIGAN

Detroit X-ray and Radium Society.—Secretary-Treasurer, E. R. Witwer, M.D., Harper Hospital, Detroit. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society club rooms, 4421 Woodward Ave., Detroit.

Michigan Association of Roentgenologists.—Secretary-Treasurer, E. M. Shebesta, M.D., 1429 David Whitney Bldg., Detroit. Meetings quarterly by announcement.

MINNESOTA

Minnesota Radiological Society.—Secretary, John P. Medelman, M.D., 572 Lowry Medical Arts Bldg., St. Paul. Meetings quarterly.

MISSOURI

The Kansas City Radiological Society.—Secretary, P. E. Hiebert, M.D., 907 North Seventh St., Kansas City, Kansas. Meetings last Thursday of each month.

The St. Louis Society of Radiologists.—Secretary, Wilbur K. Mueller, M.D., University Club Bldg. Meets on fourth Wednesday of each month except June, July, August, and September, at a place designated by the president.

NEBRASKA

Nebraska Radiological Society.—Secretary, D. A. Dowell, M.D., 816 Medical Arts Bldg., Omaha. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

NEW ENGLAND

New England Roentgen Ray Society (Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island).—*Secretary,* Hugh F. Hare, M.D., Lahey Clinic, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

NEW JERSEY

Radiological Society of New Jersey.—Secretary, H. J. Perlberg, M.D., Trust Co. of New Jersey Bldg., Jersey City. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called by president.

NEW YORK

Associated Radiologists of New York, Inc.—Secretary, William J. Francis, M.D., 210 Fifth Ave., New York City. Regular meetings the first Monday evening of the month in March, May, October, and December.

Brooklyn Roentgen Ray Society.—Secretary-Treasurer, Leo Harrington, M.D., 880 Ocean Ave. Meetings held the fourth Tuesday of every month, October to April.

Buffalo Radiological Society.—Secretary-Treasurer, Joseph S. Gianfranceschi, M.D., 610 Niagara St. Meetings second Monday evening each month, October to May, inclusive.

Central New York Roentgen Ray Society.—Secretary-Treasurer, Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse. Meetings are held in January, May, and October, as called by Executive Committee.

Long Island Radiological Society.—Secretary, Marcus Wiener, M.D., 1430 48th St., Brooklyn. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—Secretary, Paul C. Swenson, M.D., Presbyterian Hospital, New York, N. Y.

Rochester Roentgen-ray Society.—Secretary, S. C. Davidson, M.D., 277 Alexander St. Meetings at convenience of committee.

NORTH CAROLINA

Radiological Society of North Carolina.—Secretary-Treasurer, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meeting with State meeting in May, and meeting in October.

NORTH DAKOTA

North Dakota Radiological Society.—Secretary, L. A. Nash, M.D., St. John's Hospital, Fargo. Meetings by announcement.

OHIO

Ohio Radiological Society.—Secretary, J. E. McCarthy, M.D., 707 Race St., Cincinnati. The next meeting will be held at the time and place of the annual meeting of the Ohio State Medical Association.

Cleveland Radiological Society.—Secretary-Treasurer, J. O. Newton, M.D., 13921 Terrace Road, East Cleveland. Meetings at 6:30 P.M. at the Mid-day Club, in the Union Commerce Bldg., on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*Secretary-Treasurer,* Justin E. McCarthy, M.D., 707 Race St. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—Secretary-Treasurer, L. E. Wurster, M.D., 416 Pine St., Williamsport. The Society meets annually.

The Philadelphia Roentgen Ray Society.—Secretary, Barton R. Young, M.D., Temple University Hospital, Philadelphia. Meetings held first Thursday of each month at 8:15 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22nd St., Philadelphia.

The Pittsburgh Roentgen Society.—Secretary-Treasurer, Harold W. Jacox, M.D., 4800 Friendship Ave., Pittsburgh, Pa. Meetings are held on the second Wednesday of each month at 4:30 P.M., from October to June, at the Pittsburgh Academy of Medicine, 322 N. Craig St.

ROCKY MOUNTAIN STATES

Rocky Mountain Radiological Society (North Dakota, South Dakota, Nebraska, Kansas, Texas, Wyoming, Montana, Colorado, Idaho, Utah, New Mexico).—*Secretary,* A. M. Popma, M.D., 220 North First St., Boise, Idaho.

SOUTH CAROLINA

South Carolina X-ray Society.—Secretary-Treasurer, Malcolm Mosteller, M.D., Columbia Hospital, Columbia. Meetings in Charleston on first Thursday in November, also at time and place of South Carolina State Medical Association.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee Radiological Society.—Secretary-Treasurer, J. Marsh Frère, M.D., 707 Walnut St., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

Texas Radiological Society.—Secretary-Treasurer, L. W. Baird, M.D., Scott and White Hospital, Temple.

VIRGINIA

Virginia Radiological Society.—Secretary, Charles H. Peterson, M.D., 603 Medical Arts Bldg., Roanoke.

WASHINGTON

Washington State Radiological Society.—Secretary-Treasurer, Kenneth J. Holtz, M.D., American Bank Bldg., Seattle. Meetings fourth Monday of each month at College Club, Seattle.

WISCONSIN

Milwaukee, Roentgen Ray Society.—Secretary-Treasurer, C. A. H. Fortier, M.D., 231 W. Wisconsin Ave., Milwaukee. Meets monthly on second Monday at the University Club.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russell F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

CANADA

Section on Radiology, Canadian Medical Association.—Secretary, W. J. Cryderman, M.D., Medical Arts Bldg., Toronto.

Section on Radiology, Ontario Medical Association.—Secretary, W. J. Cryderman, M.D., 474 Glenlake Avenue, Toronto.

Canadian Association of Radiologists.—Honorary Secretary-Treasurer, A. D. Irvine, M.D., 540 Tegler Bldg., Edmonton, Alberta.

La Société Canadienne-Française d'Eléctrologie et de Radiologie Médicales.—General Secretary, Origène Dufresne, M.D., Institut du Radium, Montreal. Meetings are held the third Saturday of each month, generally at the Radium Institute, 4120 East Ontario Street, Montreal; sometimes, at homes of members.

CUBA

Sociedad de Radiología y Fisioterapia de Cuba.—Offices in Hospital Mercedes, Havana. Meetings are held monthly.

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ROENTGEN DIAGNOSIS

THE CHEST

Roentgenologic Considerations of Bronchiectasis. Eugene P. Pendergrass. Arch. Otolaryng. **34:** 974–990, November 1941.

This paper is one of a symposium dealing with various aspects of bronchiectasis. The author considers first the normal roentgen appearances of the chest and the effect of the phases of respiration upon these, going on to a discussion of bronchography, which is necessary to furnish the surgeon and bronchologist with the information which they require for treatment. Bronchography is always preceded in the author's practice by roentgen examination of the neck, chest, and esophagus. It is thus possible to diagnose or exclude any esophageal lesion that involves the adjacent mediastinal structures by direct invasion or any lesion, such as preventriculosis, that allows retained contents to be aspirated into the lungs from the filled esophagus.

The bronchographic technic given here is described as the bronchoscopic or direct method. After anesthetization of the pharynx, bronchoscopy is performed, and during this the trachea and larger bronchi are anesthetized and the secretions aspirated. Immediately after the removal of the bronchoscope, a soft rubber catheter with a curved metal tip is passed into the nose, directed into the larynx and trachea, and fixed in place. The patient is then taken into the fluoroscopic room, and an opaque medium is instilled during fluoroscopic examination. The preliminary aspiration allows the opaque material to enter any and all parts of the lung. During the fluoroscopic observation films are made by the "flash" technic with the subject in various anteroposterior, rotated, and lateral positions, and in various phases of respiration, in order to obtain a permanent record of the pertinent fluoroscopic observations. Both lungs may be studied at one sitting, but the author prefers to study one at a time with an interval of several days. For a child's lung 10 c.c. of opaque oil are sufficient; 20 to 30 c.c. are required for one lung in an adult. After the fluoroscopic examination, the catheter is withdrawn, and conventional roentgenograms are made of the chest in predetermined positions.

The points to which special attention is given are the location and extent of the disease process, the structure of the bronchial tree, and the condition of the flexible elements (muscle, cartilage, and elastic fibers), the degree of fixation, and the time required for the lung to drain. The condition of the flexible elements is of special importance in the decision between conservative and radical therapy. If the flexible elements are destroyed, only lobectomy will effect a cure. The roentgen evidence that they are intact is the change in the diameter and the length of the bronchi during respiration: increase in size and elongation at the end of inspiration; decrease in size and shortening at the end of expiration. Changes in size and length will also occur during coughing.

The Post-Operative Complications of Pulmonary Lobectomy: Clinical and Experimental Study. F. J. Sambrook Gowar. Brit. J. Surg. **29:** 3–18, July 1941.

Pulmonary lobectomy as a curative operation in certain cases of bronchiectasis carries a mortality of from 10 to 20 per cent. The postoperative complications are shock, reactionary hemorrhage, tension pneumothorax, embolic phenomena, intracardiac thrombosis, massive collapse of the remaining lobe, bronchopneumonia, infection, pericarditis, and spread of bronchiectasis.

Massive collapse of the remaining lobe is the most serious of the complications of lobectomy and was responsible for one-third of the total postoperative deaths in this series of 154 cases. Bronchopneumonia is more likely to occur if bronchiectatic areas of lung remain after operation, and is one of the greatest dangers when operating in the presence of bilateral disease. Infection may occur in the hilar stump or in the chest wall.

In an uncomplicated case with free upper lobe the remaining lobe expands rapidly, is well out in twenty-four hours, and expansion is complete in three to five days. Various factors are necessary to bring about this desirable state of affairs, notably a free outlet for fluid and air from the pleural cavity as the lobe re-expands; freedom of the bronchial tree from obstruction; maintenance of a negative intrapleural pressure by the inspiratory chest movements and the closed (water seal) drainage system.

There is an excellent detailed description of the factors responsible for collapse, with numerous illustrations. The preoperative use of iodized oil is discussed and there are indications that an interval of eight weeks or more is desirable between bronchography and lobectomy. The presence of pleural adhesions is a favorable factor in prevention of upper lobe collapse and in some cases artificial pleurodesis was performed. Some experimental studies along this line are briefly recorded. Spinal anesthesia was found to be the most satisfactory provided certain postural precautions were taken postoperatively to aid venous return from the limbs.

MAX CLIMAN, M.D.

Giant-Cell Tumor of the Trachea. J. M. Cid and J. Lopez Bonilla. J. Thoracic Surg. **11:** 210–215, December 1941.

This report from Argentina concerns a giant-cell tumor of the trachea in a man of 25, whose chief complaints, dating back to a severe cold six months previously, were a whistling sound in the chest, dyspnea, cough, and hemoptysis. On admission the patient brought several chest films, taken elsewhere. In the earliest of these a dense shadow was apparent at the base of the right lung, and a small pneumothorax extended from apex to base; there was a small but unmistakable fluid level. In the later roentgenograms a gradual decrease of these abnormalities was evident. A film taken by the author four months after the earliest film showed that the dense basal shadow had disappeared, but the zone where the shadow had previously been evident, and, in fact, the entire lower lobe, were more clear than the opposite lung, so that the bronchovascular markings could hardly be seen.

Symptoms, clinical signs, and roentgenological appearance combined to suggest the existence of an intrabronchial tumor. Bronchoscopic biopsy was attempted but induced severe hemorrhage and the patient died with massive collapse of the right lung and mediastinal emphysema.

At necropsy the tumor was found chiefly in the right main bronchus. It measured $2 \times 5 \times 4$ cm. and rested on a somewhat smaller base directly on the carina. Microscopic sections showed a varied picture, with areas of loose mucoid character, others of a fibrous and osteofibromatous structure, and still others of multinuclear cells. This latter type of cell was by far the most constant and extensive and was considered to be the basic element of the tumor. The growth had its origin from a tracheal cartilage, which in one small area had become ossified.

A review of the literature failed to disclose any previous report of a giant-cell tumor of the trachea. The author explains its rarity by the fact that giant-cell tumor is essentially a bone tumor and the trachea does not tend to ossify even in old age.

H. O. PETERSON, M.D.

Choosing a Method for Mass X-Raying of Service Men. Nelson Mercer. Mil. Surgeon **89:** 772–776, November 1941.

Of the various methods which have been suggested for the mass roentgen study of men in the military and naval services the author regards the rapid paper film method as the one of choice. While it is true that the cost of the film is greater—about 25 cents for each 14 × 17-inch roentgenogram, as compared to one cent per exposure for 35-mm. film and 5 cents per exposure for 4 × 5-inch film—this difference, he believes, is offset by the greater accuracy of the larger roentgenograph. [For a review of the various methods and the generally accepted views as to their relative merits, see the editorial in a recent issue of RADIOLOGY (**38:** 498, April 1942).]

THE DIGESTIVE TRACT

The Gastrointestinal Tract in Hyperthyroidism. Robert B. Brown, E. P. Pendergrass, and E. Douglas Burdick. Surg., Gynec. & Obst. **73:** 766–783, December 1941.

Attention is called to digestive disturbances in hyperthyroidism, which are often overshadowed by cardiovascular, neuromuscular, or ocular manifestations. Possible evidences of a hyperthyroid state, referable to the gastro-intestinal tract, include increased appetite, nausea and vomiting, diarrhea, and even abdominal pain.

Twenty-four clear-cut cases of hyperthyroidism with a comparable control series of 14 normal persons were considered from the standpoint of gastric secretion and gastro-intestinal activity. In all of the 24 hyperthyroid cases thyroid resections were subsequently done and comparative postoperative studies were carried out. For gastric analysis six specimens were taken, the first half an hour following administration of the test meal and the remainder at fifteen-minute intervals thereafter. If free hydrochloric acid was not found in the first two specimens, histamine was injected subcutaneously before further samples were taken. Gastro-intestinal motor activity was studied by roentgen examination after the ingestion of a barium water mixture, and numerous roentgenograms are reproduced. Methods of statistical analysis were used to evaluate the results.

Comparison of controls with the preoperative hyperthyroid group indicated that the following gastro-intestinal changes are characteristic of hyperthyroidism: (1) increased incidence of achlorhydria; (2) increased prominence of gastric rugae; (3) an increase in the rapidity with which the stomach starts to empty (of questionable significance); (4) a delay in final gastric emptying; (5) increased small intestinal tone with an abnormally fine mucosal pattern; (6) increased small intestinal motility; (7) increased large intestinal tone; (8) increased large intestinal motility. Attention is drawn by the authors to the difficulties in judging some of the changes in intestinal tone, pattern, and motility, especially the possible influence of psychic factors on the latter. Vitamin B complex deficiency is considered as a possible etiological factor in the production of gastro-intestinal abnormalities in patients with hyperthyroidism.

[Some of the above conclusions are not strongly supported by the authors' own figures and analyses.—I. J. M.] IVAN J. MILLER, M.D.

Diaphragmatic Hernia with Penetrating Ulcer of Herniated Stomach. L. Wallace Frank and Joseph E. Hamilton. J. Thoracic Surg. **11:** 219–226, December 1941.

A case of diaphragmatic hernia is reported occurring in a 57-year-old male negro. Four years earlier the patient was shot through the left chest and recovered uneventfully. There were no symptoms of the hernia until three days before admission, when he was awakened from sleep by abdominal discomfort and swelling, dyspnea, and aching pain in the left chest, arm, and shoulder. He suffered also from hiccoughs, nausea, and vomiting. A presumptive diagnosis of coronary occlusion was made, but this was not substantiated by an electrocardiogram. A chest film showed what was considered to be a marked elevation of the left side of the diaphragm. Later barium meal examination revealed a hernia of the fundus of the stomach through the diaphragm, though the colon was in normal position. Resection of 1.5 inches of the phrenic nerve relieved the shoulder pain, but five months later severe pain developed in the left chest. A barium meal study now showed a large penetrating gastric ulcer in the herniated part of the stomach and herniation of the transverse colon into the thorax. At operation the ulcer was found to be adherent to the aorta and, since it could not be separated, the stomach was trimmed away. The stomach and colon were returned to the abdomen and the defect in the diaphragm was repaired. Convalescence was uneventful.

The diaphragmatic defect in this case began just to the left of the esophageal hiatus and extended anteriorly and laterally. It did not correspond, in position, to the congenital hernias or the hiatus hernias, and was considered to be traumatic.

The authors believe this case unusual, since they have found no previous report where an ulcer had to be resected along with repair of a hernia. There was no atrophy of the diaphragm, even though the phrenic nerve had been sectioned five months earlier and no accessory branches were believed to be present. It is suggested that possibly the intercostal innervation of the diaphragm was acting in a compensatory manner.

Hiatus hernias should be treated symptomatically in most instances, and traumatic and congenital hernias should be corrected surgically.

H. O. PETERSON, M.D.

Subcostosternal Diaphragmatic Hernias. Foramen of Morgagni. Stuart W. Harrington. Surg., Gynec. & Obst. **73:** 601–614, November 1941.

Subcostosternal diaphragmatic hernia, *i.e.*, herniation of the abdominal viscera through the foramen of Morgagni or Larrey's space in the anterior portion of the diaphragmatic muscle into the thoracic cavity, has long been known, but has only rarely been reported in the literature. The number of cases was given as 58 by Funck-Brentano in 1933 (Ann. d'anat. path. **10:** 401, 1933). The author has found 24 cases reported since 1930, in 5 of which operation was performed. In his own experience only 4 examples were encountered in 270 operations for diaphragmatic hernia of various types.

These are essentially direct hernias through a congenital defect in the structure of the diaphragm or a faulty attachment of the diaphragm to the sternum and costal cartilages. Like esophageal hernias, they are rarely present at birth, occurring in later life as a result of increased abdominal pressure on the congenitally defective diaphragm.

In cases in which hollow viscera are involved in the hernia, symptoms occur which suggest the diagnosis or at least the necessity of roentgen study of the intestinal tract, which will be conclusive. The cases in which only the omentum is involved present a more difficult diagnostic problem. The subjective symptoms, which are entirely thoracic as a result of mechanical interference with respiration and expansion of the lungs, suggest the presence of a pulmonary lesion and roentgen examination appears to confirm this.

Complete reports are given of the author's 4 cases, with numerous illustrations. All the patients were

adults and in none was a history of trauma obtained. In each case a complete hernial sac extended into the right thoracic cavity. The contents of the sac were omentum only in 2 cases (both in women), each of which was diagnosed clinically and roentgenologically as a primary intrathoracic tumor, the results of gastrointestinal examination being negative. In one of these patients exploratory thoracotomy established the true diagnosis and in the other operation for an associated esophageal hiatus diaphragmatic hernia revealed the presence also of a subcostosternal hernia. In the other 2 cases, in men of thirty-four and twenty-seven years, the contents of the hernial sac were omentum and transverse colon, and omentum, terminal ileum and cecum, respectively. These patients presented the usual symptoms of intermittent digestive disturbances and partial intestinal obstruction.

The surgical approach for repair of the subcostosternal hernias was through a right rectus abdominal incision in all 4 cases, and the defect in the diaphragm was closed with living suture of fascia lata stabilized with silk sutures.

The hernial sac was excised in 2 cases and left *in situ* in 2 cases. There were no operative deaths and there have been no recurrences. [The author does not include a bibliography. Colmers' paper in Radiology **37:** 733, 1941, may be consulted for references to the literature.]

Pneumogastroscopy. A Preliminary Report. A. S. D'Eloia. Am. J. Surg. **53:** 280–283, August 1941.

A technic is described for visualization of the interior of the stomach, for which the authors claim many advantages, with none of the disadvantages of the opaque meal. It involves the use of a specially designed tube carrying a balloon, which is insufflated with air to expand the stomach, and a separate water ballast to prevent over-expansion of the duodenum.

Tumours of the Small Intestine. J. Edgar Morison. Brit. J. Surg. **29:** 139–153, July 1941.

A review of a large number of autopsies and biopsy specimens yielded 21 primary tumors of the small intestine. There were 5 lipomata, 3 adenomata, 2 leiomyomata, 1 pedunculated subserous fibroma, 2 carcinoid tumors, 4 adenocarcinomata, and 4 lymphosarcomata. Two of the lipomata produced intussusception and the remaining 3 occurred almost at the ileocecal valve. Two of the latter were associated with edema and non-specific inflammatory changes in the wall of the terminal ileum and cecum. Many of the cases of carcinoma reported have been accepted as primary tumors on an inadequate basis. This is especially so in the duodenum. The frequent reports of tumors ulcerating the duodenum and extending into the pancreas suggest that many of these neoplasms may be primary in the latter organ. In this series 4 patients presented conclusive evidence of primary cancer involving the small intestine: 2 in the upper and lower jejunum and 2 in the ileum. The lymphosarcomata infiltrate the wall of the intestine and may produce a saccular dilatation.

Radiological examination was made in 9 cases with diagnosis suggested in only 4 cases. The clinical findings of importance were those of partial or complete obstruction. Vomiting occurred earlier and was more frequent than in colonic new growths. A palpable mass was present in 2 of the 3 cases of intussusception and 4 of the other cases. MAX CLIMAN, M.D.

The Terminal Common Bile Duct and Duodenal Papilla: A Roentgenological Consideration. Maurice Feldman. Surg., Gynec. & Obst. **73:** 838–844, December 1941.

The author states that there is an apparent lack of knowledge of the roentgenologic anatomy of the interior of the descending portion of the duodenum. He believes the study of this segment of the bowel important in relation to pathological conditions in the terminal common bile duct and duodenal papilla, and that proper interpretation of minimal changes in outline of the second portion of the duodenum will contribute to the correct diagnosis of disease in these closely related parts. He states categorically that lesions in the terminal common bile duct and duodenal papilla invariably affect the duodenum.

After a description of the normal roentgenologic appearance of the descending duodenum, based on fluoroscopy and serial roentgenograms, 10 roentgenologic signs of disease of the terminal common bile duct and major duodenal papilla are listed as follows: "(1) enlargement and broadening of the plicae longitudinalis duodeni fold, (2) encroachment of the enlarged duodenal fold upon the lumen of the duodenum, (3) mucosal changes in the pattern of the [duodenal] ampullary mucosa, (4) enlargement of the major duodenal papilla, (5) filling defect in the contour of the duodenum, (6) varying degrees of stenosis, (7) secondary ulceration producing a defect, (8) invasion of the pancreas which may produce signs of pancreatic pressure on the contour of the duodenum, (9) cholecystographic changes, producing non-filling of the gallbladder when the bile duct is occluded, (10) pressure defect of the stomach in late cases."

Nine roentgenograms are reproduced.

[The terminology used in this article is not always clear. For example, the expression used in the first listed sign of disease literally means "the fold of the longitudinal fold of the duodenum." We trust the author will clarify these points in subsequent publications on this subject.—I. J. M.]

IVAN J. MILLER, M.D.

THE SKELETAL SYSTEM

Fractures of the Malar and Zygoma. Frederick R. Corbin. Mil. Surgeon **89:** 750–754, November 1941.

Fractures of the malar bone are usually the result of direct force. As a rule, the fracture line involves one of the four processes of the bone—the frontal, orbital, maxillary, or temporal, the body of the bone being displaced rather than fractured.

Because of the location and form of the malar bone and zygomatic arch, roentgen study requires a special technic if it is to be of diagnostic value. The author suggests the following: ". . . . place on a table the cassette holding the film in a position parallel to the floor. The patient should then be placed so that the edge of the cassette touches the clavicle, with the patient's head extended to have the anterior surface of the neck and chin in contact with the cassette, the mean plane of the head being as nearly perpendicular to the cassette as possible. The tube is placed above the head so that the rays are directed downward paralleling the plane of the face and paralleling the sagittal plane. It sometimes may be necessary to shift the tube to the right or left of the sagittal plane to obtain a more detailed study of the injured part."

Various methods of treatment are mentioned. The most universally accepted is external reduction by means of an incision in the temporal region.

Intracapsular Fractures of the Neck of the Femur: Final Results of 75 Consecutive Cases Treated by the Closed Method of Pinning. A. L. Eyre-Brook and K. H. Pridie. Brit. J. Surg. **29:** 115–138, July 1941.

This is an analysis of 75 consecutive cases of fracture of the neck of the femur which have been treated by the closed method of introducing the Smith-Petersen pin. All the cases were followed for a minimum period of twelve months. Successful results were obtained in 38

cases. A period of three months was adopted as the time during which no weight-bearing was allowed. An angle formed by the fracture line and the axis line of the *shaft* of the femur is used as an index of the inherent tendency of the fracture to slip. This angle is read with ease on the anteroposterior film. A lateral view showing the angle subtended by the fracture line to the *neck* of the femur is also necessary. There was no complication in any case having a fracture-shaft angle greater than 37°. When the angle is below 30° some modification of the Smith-Petersen pinning, either the addition of a bone-graft or a subtrochanteric osteotomy, to increase the angle, ought probably to be employed.

The failures were due to necrosis, failed pinnings, fibrous union, pin penetration, and suppuration. The incidence of necrosis varies inversely with age; in all cases with this complication the fracture-shaft angle was below 37°. The radiographic signs of necrosis preceding collapse consist of increased density, lack of distinct trabeculations, and mottling. There were 10 cases of fibrous union. All of these showed a slight shift at the fracture site in the early roentgenograms, which is often the cause of fibrous union. Pin penetration occurred in 4 cases, in 3 of which union was never definitely bony. There were 3 cases of suppuration, all in old and debilitated patients. MAX CLIMAN, M.D.

Trochanteric Fractures. Harry D. Morris. South. M. J. **34:** 571–576, June 1941.

A method of internal fixation is advocated for trochanteric fractures, using the Smith-Petersen nail and the Thornton plate together. The method is considered especially useful for charity hospitals since it minimizes nursing care. The patient can be placed in a wheel chair a few days after operation and becomes ambulatory in three or four weeks.

The technic of the operation is described. Local anesthesia is employed. Preoperatively, a roentgenogram is made of the sound hip, with a marker at the level of the greater trochanter to estimate accurately the length of the nail necessary. After the nail is introduced, anterior-posterior and lateral roentgenograms are made, and, if the position is satisfactory, the Thornton plate is applied. Exposure of the trochanteric region frequently reveals more comminution than is apparent in the preoperative roentgen film.

JOHN M. MILES, M.D.

Radiographic Evaluation of Healing Fractures. John L. Dixon. Mil. Surgeon **89:** 796–798, November 1941.

Uncomplicated bone fractures show four stages to complete healing, which may be recognized roentgenographically: (1) no callus; (2) insufficient callus for restricted use; (3) sufficient callus for restricted use; (4) sufficient callus for unrestricted use.

Callus first appears in fourteen to twenty-four days in the normal adult, and earlier in the child. The first roentgen evidence of its presence is a light homogeneous or flocculent and amorphous shadow extending out from each fragment. At the same time there is decalcification of the adjacent injured bone on both sides of the fracture; the fracture line has begun to lose its sharp appearance but is still plainly visible. This is the second stage in the author's classification: insufficient callus for restricted use. Under normal conditions, stage 3 rapidly follows: the callus increases in amount, bridging the fracture and becoming more dense until it begins to approach the adjacent normal cortex both in amount (cross-section of the cortical bone on both sides and intervening trabeculations) and density (degree of opacity as compared with the opacity of the normal adjacent cortex on the roentgen film). The fracture line is now indistinct and fading. In time the callus exceeds the normal cortex and intervening trabeculae both in size and density, placing the fracture in stage 4.

Slipping of the Upper Femoral Epiphysis. M. Beckett Howorth. Surg. Gynec., & Obst. **73:** 723–732, November 1941.

This paper is based upon a study of 132 cases of slipping of the upper femoral epiphysis. The incidence was found to be slightly greater in boys than in girls; 65 per cent of the patients were tall or overweight. Trauma sometimes served to call attention to the condition but is not an etiologic factor.

Four stages are recognized: preslipping, slipping, quiescent, and residual. The onset of the preslipping stage is usually gradual, with a limp or pain or both. The roentgenologic features at this stage, as observed in this series, were widening and irregularity of the epiphyseal line, with decalcification of the proximal end of the neck. The head was not visibly affected. The capsule was usually swollen. The transition to the slipping stage may be acute or gradual. The roentgenogram reveals the degree of slipping. The typical deformity is a downward and backward displacement of the head with adduction (varus). In some cases, there is only posterior displacement, while in others the downward displacement is much greater than the posterior. The degree of posterior displacement may best be seen in the lateral view. Callus forms in the inferior and posterior interval between the head and neck and may be seen soon after the slip. In many cases two or more layers of callus are present, indicating that two or more slips have occurred.

As the lesion becomes quiescent in either the preslipping or slipping stage, the epiphyseal line begins to assume its normal width and regularity, and the proximal end of the neck recalcifies. The callus soon becomes mature. The proximal margin of the neck superiorly loses its angular appearance and becomes smooth and level with the head. After several months or years, depending upon the age of the patient, the epiphyseal line becomes ossified, thus reaching the residual stage at about the age of sixteen in girls and eighteen in boys. When there is much displacement, arthritic lipping at the head usually supervenes, and later it may involve the acetabulum.

Clinically and pathologically the condition is found to be primarily a synovitis occurring during the period of rapid growth and producing circulatory changes in the epiphyseal disc, resulting in decalcification and softening. The slipping is the result of weight-bearing or mild injury to the softened epiphyseal junction.

The lesion eventually heals regardless of treatment. The aim of the latter is to secure a painless hip, free of limp, with full motion and full capacity for normal activity. Correction of deformity in the quiescent and residual stages is preferably by subtrochanteric osteotomy, a procedure which the author has used in 6 cases with fairly satisfactory results. In the slipping stage reduction of the deformity is desirable when there is half an inch or more of displacement downward or posteriorly. Closed reduction has been attempted but with unsatisfactory results. Reduction by strong traction followed by internal rotation and immobilization in plaster has also been employed, as has open reduction, with fair results. The most satisfactory treatment is in the preslipping stage. Rest and freedom from weight-bearing if sufficiently prolonged will lead to healing in this stage, but immobilization in plaster is contraindicated. To hasten the healing the author uses a drilling operation with excellent results.

Leontiasis Ossea. George K. Kirkland. Brit. J. Surg. **29:** 74–83, July 1941.

Leontiasis ossea was the name given by Virchow in 1896 to hyperostosis of the facial and cranial bones.

The earliest pictures of the disease were based largely on the skulls in museum collections and were very incomplete. Very few cases have been reported, due to the difficulty of separating the condition as a distinct clinical entity from other bone diseases, in particular Paget's osteitis fibrosa. The author reports 2 cases.

The first patient was a man aged 54 with a huge, grossly deformed head. The facial bones were more affected than the calvarium. The right maxilla alone was missed by the disease. Roentgenograms of the skull showed massive overgrowth of new bone. The second case was in a female aged 25, who complained of severe headaches and insomnia. Her first x-ray examination showed involvement of the frontal and maxillary bones. After an interval of two years there was more involvement of the right frontal bone, with extension into the left parietal bone. Neither patient presented any evidence of mental abnormality. The laboratory data were negative in both cases except for increase in phosphatase activity. This finding has led some authors to believe that leontiasis ossea is actually Paget's disease. In Paget's disease, however, the skull is more likely to be involved than the face, whereas in leontiasis ossea the reverse holds. The disease usually begins insidiously, often in late childhood or adolescence. In the great majority of cases no treatment is beneficial. Operation has frequently been undertaken for pressure symptoms, particularly for nasal obstruction, pressure on the orbit, and epilepsy from enostoses.

MAX CLIMAN, M.D.

Congenital Proximal Radio-Ulnar Synostosis. S. V. Humphries. South African M. J. **15:** 486, Dec. 13, 1941.

Radio-ulnar synostosis, or congenital fusion of the proximal ends of the radius and ulna, is only rarely encountered in man, though normally present in certain vertebrate animals. Prominent among the symptoms is inability to supinate the hand. The condition is considered to be of congenital origin, and a familial history is not unusual. In about half the cases the deformity is bilateral. There are two main types. In one the radial head is absent, the proximal end of the radius being fused with the ulna; in the other the head of the radius is displaced toward the flexor surface of the arm. The extent of bony union varies from about 2 to 6 cm.

The radius and ulna develop from the same precartilage plate, and, at a later stage, the perichondrium of the two bones is continuous at their proximal ends, though the distal ends are separated from each other by condensed tissue continuous with the perichondrium of each. Synostosis is presumably due to some alterations of the chromosomes. There is probably a gene mutilation that alters the various developmental impulses that direct the formation of the proximal ends of the bones of the forearms. That abnormal developmental impulses exert some influence is also suggested by the fact that other bony defects often occur in the patient or in his relatives. These include exostoses, club-foot, club-hand, flat-foot, and other conditions associated with a dyschondroplasia.

Males are affected twice as often as females, and the condition occurs in families where there are consanguineous matings.

A case is reported and roentgenograms are reproduced, showing entire absence of a radial head. The upper ends of the bones are fused for a distance of about 5 cm., but there is no fusion of the shafts or distal ends.

PERCY J. DELANO, M.D.

Senile Osteoporosis of the Spinal Column. John R. Black, Ralph K. Ghormley, and John D. Camp. J. A. M. A. **117:** 2144–2150, Dec. 20, 1941.

This report is based on a study of 208 patients, 167 women and 41 men. The average age of all, when first seen, was 62. Senile osteoporosis is definitely associated with the older age groups. The number of women afflicted is about four times the number of men. This may be because the life expectancy of women is greater than that of men, and they lead a more sedentary life. Osteoporosis, however, does afflict persons who have always been extremely active.

The usual history begins with weakness, fatigue, or a dull ache in the lower part of the back at about the age of fifty-nine. This early stage usually lasts several years. Then, as a result of trauma, which may consist in nothing more than lifting or bending, there is a sudden snap or acute pain in the back. The patient often is forced to go to bed. Sharp agonizing pains occur on the slightest movement. The pain is chiefly in the lower thoracic area and in the lumbar region. Frequently it is projected along the nerve roots. There may be associated sciatica. It is rare, however, to find any neurologic signs, such as changes in sensation or reflexes. The occurrence of mild trauma as the primary agent in the onset of acute symptoms has been ascribed to pre-existing osteoporosis in which trauma has produced collapse of a vertebra and severe pain. The pain is aggravated by lifting, coughing, or sneezing. Other symptoms are weakness, easy fatigue, and nervousness.

On physical examination, the patients present all the signs of senility, general atrophy of the tissues, and arteriosclerosis. Frequently they are thin and emaciated. The back is rounded. The gait is careful, to avoid jarring. There is usually marked limitation of motion of the spinal column, due to muscle spasm. Tenderness on pressure over the spinous processes is not severe or well localized.

A total of 92 determinations of serum calcium were carried out in 68 cases. The average value was 9.8 mg. of calcium per 100 c.c., with a range from 7.8 to 12.7 mg. Inorganic phosphorus determinations showed a mean value of 3.4 mg. per 100 c.c., with a variation from 2.1 to 6.5 mg. The mean value in phosphatase determinations was 3.8 Bodansky units, with a range from 2 to 13.4 units. In one case in which there was an elevated concentration of serum calcium exploration of the parathyroid glands failed to reveal a tumor or hyperplasia. In 2 cases of extensive osteoporosis with chemically normal blood constituents, exploration showed the parathyroid glands to be normal, in agreement with the reports on similar cases by other authors.

Gross Pathologic Changes: Senile osteoporosis, involving as it does primarily the trabeculae of spongy bone, is most evident in the vertebrae. The cortical bone is much thinner than normal, and there is enlargement of the marrow spaces and the medullary cavity. The trabeculae are thinner and fewer than normal, but their architectural arrangement is maintained. When osteoporosis has progressed to a certain degree, the trabeculae are no longer able to resist the weight of the body and the internal pressure of the intervertebral disks. There occur a collapse of the central portions of the vertebral body and expansion of the nucleus pulposus and disk. The vertebral bodies may collapse in their anterior part, as in a true compression fracture.

Degenerative disk changes occur usually in the upper thoracic region and lead to thinning of the disks, hypertrophic changes about the anterior margins of the vertebral bodies, and dorsal kyphosis. The phenomenon of ballooned disks is more often seen in the lower thoracic and lumbar regions.

Roentgenologically Apparent Changes: The intervertebral disks in the lower thoracic and the lumbar regions were the ones most frequently involved in the authors' series. In general, the degree of expansion of the disks and the number of vertebrae compressed depend on the grade of osteoporosis. In some patients, all the disks in the thoracic and lumbar regions were ballooned and many vertebrae were crushed.

The cause of the backache and of the sharp radiating pains in osteoporosis is not entirely clear. The most satisfactory explanation is that the pain is a reflex one that arises from the recently compressed vertebrae and is referred along the nearby nerve roots. It is not due to pressure on the nerve roots because the foramina are usually free.

It is the authors' impression that in the syndrome of senile osteoporosis of the spinal column, the osteoporosis attains its greatest degree in the vertebrae, and this was borne out by a series of cases in which the long bones of the extremities were also studied roentgenographically.

Differential Diagnosis: Hyperparathyroidism produces a generalized osteoporosis described by Bauer and Camp, by Camp, and by Camp and Ochsner as a peculiar miliary mottling and granular appearance best seen in the flat bones. This characteristic osteoporosis and the subperiosteal decalcification, bowing, fractures, and cyst formation in the long bones are in most cases easily distinguished from the homogeneous osteoporosis in the flat bones and the slight changes in the long bones seen in cases of senile osteoporosis. The results of laboratory tests frequently will confirm the diagnosis. Concentration of serum calcium is usually 11 mg. or more per 100 c.c., and the concentration of inorganic phosphorus in the serum is lowered, whereas the value for serum phosphatase is usually high. The final test is a marked increase in the urinary excretion of calcium and phosphorus. These values are all within normal limits in senile osteoporosis.

In hyperthyroidism the diagnosis is made on the basis of the clinical history and findings of exophthalmic goiter.

In pituitary basophilism and adrenocortical syndromes the age of some patients and such physical observations as obesity, hypertension, hirsutism, and abdominal striae, with changes in the primary and secondary sex characteristics, serve as distinguishing features.

Osteoporosis caused by infiltration of malignant tumor cells is often homogeneous in its distribution. Rapid sedimentation of erythrocytes, in the absence of infection or other causative factors, is diagnostic of generalized carcinomatosis. The blood smear also frequently shows immaturity of the myeloid cells, the so-called leukemoid reaction.

Multiple myeloma, in addition to osteoporosis of the spine, usually produces localized evidence of destruction in the ribs, pelvis, and most clearly of all in the skull. The pain is more severe. Secondary renal changes are common. Bence-Jones protein is sometimes found in the urine.

Extensive osteoporosis is frequently seen in the spinal column and around the involved joints in cases of chronic infectious arthritis. Involvement of other joints usually helps to differentiate this disease from senile osteoporosis of the spine.

Early spondylitis deformans produces mild osteoporosis. Destructive changes in the sacro-iliac joints and intervertebral facets, with beginning calcification of the spinal ligaments, indicate the presence of this disease. Examination of the blood frequently reveals evidence of secondary anemia and an increased sedimentation rate. In senile osteoporosis there is no joint destruction nor calcification of the ligaments, nor is there an increased sedimentation rate.

Osteomalacia is the adult equivalent of the rickets of children. The concentration of calcium in the blood is high, as in rickets. Changes in the spine may resemble senile osteoporosis, but as a rule there is a marked distortion of the bony pelvis, and the long bones are involved to a greater extent. Symmetrical areas of decalcification or pseudo-fractures of the long bones occur in osteomalacia.

Etiology: Many hypotheses have been proposed to explain the onset of senile osteoporosis, the more important of which may be listed as follows: dietary deficiency, gastric achlorhydria, endocrine imbalance, and inactivity. The present study indicates that achlorhydria may be a factor but that in the majority of cases other factors are responsible. Parathyroid glands have been found normal in three cases in which they were explored. There has been little evidence to support the theory that proliferation of the basophilic cells of the pituitary gland in old age causes osteoporosis. In three cases of pernicious anemia, malnutrition and achlorhydria may have affected the absorption of calcium. In 8 cases of diabetes mellitus, acidosis or dietary regulation may have interfered with the calcium metabolism. Poor general health might have been an etiologic factor in many cases of osteoporosis seen by the authors.

Treatment: The object of therapy in cases of senile osteoporosis is threefold: first, to relieve the severe pain; second, to prevent further deformity; third, to promote recalcification of bone. Tribasic calcium phosphate with adequate amounts of vitamin D are given by the authors; 10,000 to 50,000 units may be used in the treatment of vitamin D deficiency states. Comparison of the patients receiving calcium and phosphorus, vitamin D, or all three drugs, with those who did not receive these essentials showed that 54 per cent of the former and only 33 per cent of the latter were benefited by treatment. Of the group treated with calcium, phosphorus, and vitamin D, the length of the treatment is important. Only 43 per cent of patients treated for less than six months were improved; 70 per cent of those treated six months or longer were improved.

Roentgenograms of 18 cases were made on an average of twenty-nine months after the beginning of treatment. In no case was there a sufficient change to enable one to say that it was due to recalcification and not to variation in the technic used in taking the roentgenogram. CLARENCE E. WEAVER, M.D.

Osteochondritis in the Stillborn. James R. McCord. Am. J. Obst. & Gynec. **42:** 667–675, October 1941.

The author of this paper, an obstetrician, has analyzed the roentgen findings in 129 negro fetuses at all stages of gestation, most of them stillborn, in an attempt to show that certain roentgenologically demonstrable skeletal changes are pathognomonic of congenital syphilis. His method of study was as follows: The diagnosis was made from the film without any knowledge of the case. If the films showed a positive or doubtful diagnosis, the babies were autopsied. The following tissues were stained by the Levaditi method: kidney, liver, spleen, lung, heart, and thymus. The bone lesions were reported as syphilitic only when the organisms of syphilis were found in the stained tissues. The roentgen diagnosis was based on the presence of typical saw-tooth serrations in the metaphyses.

In 91.5 per cent of the series the roentgen diagnosis of syphilis was confirmed by the finding of the organisms. A review of the 11 films incorrectly diagnosed showed absence of the typical serrations in 9. One case, though apparently typical, showed no organisms, and in one case the fetus weighed only 320 gm., as compared with an average for the series of 816 gm.

In a group of 88 cases in which the roentgen diagnosis was confirmed, 94 per cent of the mothers gave positive serologic tests, while in a control series of 321 negative films the percentage of negative maternal serology was 80, from which the author concludes that caution should be exercised in diagnosing congenital syphilis of the bones when the mother gives a negative reaction. He points out also that a roentgen diagnosis should not be attempted on fetuses weighing less than 500 gm.

In discussing this paper Dr. G. D. Royston called attention to the fact that Ludwig Pick, more than twenty-seven years ago, taught that osteochondritis of the long bones was pathognomonic of syphilis.

The Medical Aspect of Ankylosing Spondylitis (Marie-Strümpell). W. W. Herrick and T. Lloyd Tyson. Ann. Int. Med. **15:** 994–1001, December 1941.

As appears from the title, this paper concerns mainly the medical aspects of ankylosing spondylitis and is written from the point of view of the internist rather than the radiologist. A section on roentgenographic findings is, however, included, reading as follows: "These are diagnostic. The initial finding is a haziness of the sacroiliac joints with an increased bone production along the joint margins which eventually leads to bony fusion. In a later phase a similar process involves the posterior intervertebral joints of a portion or of the entire spine. In the most advanced stage there is a calcification of the anterior and lateral ligaments of the spine producing the typical bamboo appearance which is pathognomonic. A general decalcification of all bones may be seen, often quite early in the disease. It is important that the clinician remember that the roentgen-ray changes characteristic of the malady may be late in appearance and that pain, stiffness and other symptoms often precede roentgenologic findings by months or years."

Dyschondroplasia of the Distal Radial Epiphysis (Madelung's Deformity) with Fusion of the Semilunar and Triangular Bones. Harry H. Alexander, Jr., and Gilbert H. Johnson. Am. J. Surg. **53:** 349–351, August 1941.

Anton, Reitz, and Spiegel (Ann. Surg. **108:** 411, 1938) found but 21 examples of Madelung's deformity in the American literature. Seven cases have since appeared, and the authors add another. Their patient, a colored woman aged 30, presented, in addition, a bilateral fusion of the semilunar and triangular bones.

Multiple Myeloma, with Special Reference to Soft Tissue Metastasis. J. L. Donhauser and W. H. de Rouville. Arch. Surg. **43:** 946–1020, December 1941.

This rather full review discusses the literature at some length. The authors note that the serum phosphatase value in myeloma does not tend to be increased, and that chemical changes in the blood are absent except for occasional increase in the globulin fraction. Hyperproteinemia is striking. Bence-Jones protein is present in the urine in about 65 per cent of patients.

Bones chiefly affected are those with the greatest red marrow content, such as vertebrae, ribs, sternum, clavicles, and skull. The kidneys show a specific type of nephrosis, arteriosclerosis, and some calcium deposits in the tubules. Some consider this disease related to the leukemias.

Tumorous involvement of the liver, spleen, lymph nodes, cardiac muscle, kidneys, tonsils, thyroid, adrenals, ovaries, meninges, and pituitary have been reported. Blood-forming tissues are, however, the favored site. Of the authors' 5 patients, 3 had soft tissue metastases and a fourth invasion of the soft tissues by direct extension from the pubis.

Although Furth succeeded in transplanting myeloma to irradiated mice, attempts to inoculate mice, rats, and hens with tissue obtained at autopsy were unsuccessful.

Differential diagnosis includes a surprisingly large number of conditions. One of the cases reported was initially diagnosed "flat foot"! Neuritis, lumbago, rheumatism, chronic nephritis, chloroma, cord tumor, renal rickets, metastatic carcinoma, metastatic hypernephroma, bone cysts, Pott's disease, Paget's disease, osteomalacia, osteogenesis imperfecta, Hodgkin's disease, xanthomatosis, fibrocystic disease, enchondroma, basophilic adenoma, osteogenic sarcoma, Ewing's endothelioma, and hyperparathyroidism have all been confused with myeloma. Suspicion should attach to any adult, especially a male, between forty and sixty, presenting any or all of the following signs: (1) mild rheumatic pain, often generalized and impossible to locate definitely, subject to acute exacerbations and remissions; (2) backache or severe thoracic pain; (3) spontaneous fracture; (4) progressive weakness and apparent anemia; (5) bony tumor, especially of a rib, clavicle, or sternum; (6) large amounts of albumin in the urine; (7) lumbar pain; (8) continued hypotension with a nephritic syndrome; (9) shortening of stature.

A rather extensive discussion of differential diagnosis is given; the most outstanding point is the lack of any symptom which is absolutely characteristic. Five cases are reported at length, with the autopsy findings.

LEWIS G. JACOBS, M.D.

Rheumatism and Arthritis. Review of American and English Literature for 1940. Philip S. Hench *et al.* Ann. Int. Med. **15:** 1002–1108, December 1941.

Attention is called to this review of the American and English literature for 1940 on rheumatism and arthritis, prepared by the Editorial Committee of the American Rheumatism Association. The bibliography of more than 600 references indicates the scope of the paper.

THE VASCULAR SYSTEM

Cerebral Arteriovenous Aneurysms. Bronson S. Ray. Surg., Gynec. & Obst. **73:** 615–648, November 1941.

Six cases of cerebral arteriovenous aneurysm are recorded in considerable detail, one with autopsy findings. While abnormal communications between extracerebral intracranial vessels, notably the internal carotid artery and the cavernous sinus, may follow trauma, the communications between the pial and cerebral arteries, with which the present paper is concerned, are probably always congenital.

The gross appearance at the operating table is unmistakable. Large, pulsating, tortuous veins, some a centimeter or more in diameter, are seen on the surface of the brain, swirls of blood showing through their thin walls with every pulsation. The arteries supplying the fistula are also enlarged, and the small connecting vessels appear as tangled masses or "nests" of closely packed pulsating arterioles and venules.

The incidence of the lesion is low. In Cushing's series of 2,023 verified brain tumors "angioma arteriale" accounted for less than 1 per cent.

In spite of the fact that these lesions are in all probability congenital, symptoms may not attract serious attention until adult life. Two of the author's patients were over forty. Convulsions occurred in all the author's cases and were the first important symptom in 3. He does not believe, however, that they are a necessary manifestation of cerebral arteriovenous aneurysm. Transient hemiparesis, frequently mentioned by others, was observed in one patient, and an unprogressive hemiparesis was present in another. Two patients complained of periodic headaches comparable to migraine, due presumably, like the latter, to dilatation of the extracranial and middle meningeal arteries, which has been shown to exist in these cases. Increased intracranial pressure was not a significant finding. In 5 cases the retinal vessels were full and tortuous on one or both sides. A bruit heard on auscultation over some part of the head, the eyeballs, and the carotid arteries in the neck, is characteristic and in conjunction with convulsive seizures or unilateral motor or sensory disturbances should suggest the diagnosis.

Changes were demonstrable in roentgenograms of the skull in all the cases here reported. These included (*a*)

questionable or slight signs of increased intracranial pressure in 2 cases; (*b*) increased vascularity of the skull (enlarged diploe) in all 6 cases; (*c*) enlarged channels for the middle meningeal arteries, also present in all, with enlargement of the foramen spinosum as well in one instance; (*d*) local atrophy due to pressure of the aneurysm in 5 cases; (*e*) cranial overgrowth, causing an enlarged head, in one case (and possibly a second). Ventriculography was done in 3 cases and encephalography in 3, and in each instance some distortion or displacement of the ventricles was demonstrable. Encephalography would appear to be a safer procedure, as introduction of the ventricular needle into one of the vessels of the aneurysm might lead to speedy disaster. Cerebral angiography is indicated to determine the extent and location of the lesion, and injections of thorotrast (in 3 cases) and diodrast (in 1 case) for this purpose were without immediate ill effects in this series.

No completely satisfactory method of treatment exists. An exploratory osteoplastic operation with decompression was performed in 4 of the author's cases. No attempt was made to remove or ligate the cerebral vessels of the aneurysm, though some of the abnormal vessels that anastomosed directly with the dural (middle meningeal) arteries were transected and also the main trunk of the enlarged middle meningeal artery was interrupted low in the temporal fossa, as a part of the decompression. The advantage of this procedure lies in the identification of the nature of the lesion, the elimination of some of the arterial supply to the aneurysm through the middle meningeal artery, and some relief of symptoms. Its disadvantage is the threat of serious hemorrhage from inadvertent tearing of the aneurysmal vessels.

In 3 cases the common and external carotid arteries on the side of the aneurysm were ligated and in addition, in 2 cases, the internal and external carotids on the opposite side were ligated 8 months and 15 months later. This type of operation may be effective in lessening the danger of spontaneous rupture and be conducive to spontaneous occlusion of some of the vessels. Ligation of the carotid arteries is far less dangerous in cerebral arteriovenous aneurysm than in other conditions because of the extensive collateral circulation.

One of the hoped for developments in a cerebral arteriovenous aneurysm is the eventual obliteration of the lesion by a process of gradual thrombosis. As a possible aid to this process the administration of x-ray radiation has justification. In a case recorded by Cushing and Bailey good results were obtained, but in the two cases of the present series in which it was used there was nothing to indicate that it produced the desired effect.

Direct surgical attack upon the cerebral lesion would seem to have little to recommend it. In one patient not included in the present series a craniotomy was performed and the walls of many of the aneurysmal vessels on the surface of the brain were coagulated with the electrosurgical unit. The caliber of all the vessels treated in this manner was greatly diminished but few vessels became completely occluded. The procedure was followed by hemiparesis and aphasia, from which there was slow but nearly complete recovery. The bruit was unaffected.

The Collateral Venous Circulation in a Case of Thrombosis of the Inferior Vena Cava, and Its Embryological Interpretation. J. A. Keen. Brit. J. Surg. **29:** 105–114, July 1941.

A report is made of a very rare case of thrombosis of the inferior vena cava found in a dissecting-room subject, a colored male, aged seventy-one. There was nothing in the clinical history which gave any explanation of the cause. The inferior vena cava was filled by a thick fibrous cord which completely blocked the vessel from its commencement to the entrance of the first hepatic vein near the diaphragm. The thrombosis with resultant fibrosis had also spread into the right common iliac vein and into both renal veins. In the interior of the organized thrombus there was a central core of calcification. A roentgenogram of the posterior abdominal wall showed that the calcified thrombus could just be distinguished against the shadow of the vertebral column. The microscopic sections indicated an organized fibrous thrombus, in a completely inactive state, with an origin which dated back many years. No deductions could be made as to pathology or starting point of the thrombosis in the inferior vena cava. There is a detailed description of the collateral circulation, which consisted mainly of a plexus of veins deep to the crura of the diaphragm and surrounding the beginning of the abdominal aorta. The embryological interpretation was based on the presence of the venous plexuses in the perinephric fat, which suggested that they represented a re-establishment of certain of the pathways of the primitive embryonic circulation. The author gives a detailed review of the literature and explanation of the collateral circulation.

MAX CLIMAN, M.D.

THE NERVOUS SYSTEM

The Dumb-Bell Tumours of the Spine. Kenneth Eden. Brit. J. Surg. **28:** 549–569, April 1941.

There are 4 main anatomical types of dumb-bell tumor of the spine: (1) the intradural and extradural, (2) intradural and extradural and paravertebral, (3) extradural and paravertebral, and (4) foraminal and paravertebral. The fourth type lies almost entirely outside the spine, with only a small extension into a vertebral foramen. The term "dumb-bell tumor" is confined to those tumors which cause pressure erosion of bone, but do not infiltrate or arise from it.

An analysis of 334 spinal tumors revealed an incidence of 32 dumb-bell tumors, 25 of which were neurofibromata. The neurofibromata and meningiomata have a close histological relationship. They are derived from a common cell, the fibroblast. Both forms of neurofibroma arise from the connective-tissue nerve sheaths, and in the multiple form the origin may be diffuse. The meningiomata arise from the connective tissue of the arachnoid and not in relation to nerve sheaths.

The dumb-bell meningiomata are uncommon and as a rule arise intradurally, but are frequently attached to and infiltrate the dura mater.

The dumb-bell neurofibromata are quite common and comprise not only an appreciable proportion of all spinal neurofibromata, but include the majority of dumb-bell tumors of all types. They originate from the part of a nerve which passes through a foramen in the dura and as the tumor grows from this diffuse origin, one lobe is formed outside and one lobe inside the spinal canal or dura mater. The lower resistance offered to the paravertebral lobe allows it to grow more rapidly than the portion inside the spinal canal. Hence the paravertebral lobe may attain much larger proportions.

Dumb-bell hemangio-endotheliomata arise in the extradural tissues, but may worm their way out of the spinal canal, through an eroded foramen, or between 2 laminae. The paravertebral tumor may then only become palpable some time after the onset of paralysis, or after the removal of the spinal tumor.

Dumb-bell ganglioneuromata differ from the others because of their tendency to arise early in life, sometimes before the vertebral column has fully developed.

Clinical Features: The dumb-bell tumors present themselves in two main clinical forms. (1) The patient may complain of a lump in the neck or in the back, with or without symptoms of paralysis. (2) There may be no lump, and the patient manifests the

picture of spine compression. Any part of the spine may be involved. In the neck, the lump appears in the posterior or anterior triangle and may displace the trachea or esophagus, or extend into the thoracic inlet and cause symptoms of compression. The only tumors in the thoracic region which are palpable are the posterior ones, lying deeply embedded in the erector spinae muscles. The mediastinal tumors, especially those of the foraminal and paravertebral type, which do not reveal their presence by producing paralysis, are frequently silent and cause no symptoms for many years. Where symptoms were present they consisted only in slight degrees of cough and dyspnea, pain in the back, root pains, or symptoms of spinal compression. In the lumbar region the lump may be palpable on the posterior abdominal wall, and in the sacral region it can be felt lying on the surface of the sacrum on rectal examination. The intradural and extradural form of dumb-bell tumor and those without a palpable paravertebral lobe have no characteristic clinical features to distinguish them from ordinary spinal tumors. When a paravertebral lobe is present, however, it is quite common for the spinal compression to improve temporarily, and later to relapse, possibly due to release of pressure within the spinal canal by the erosion of a foramen and the subsequent further growth of the spinal portion, with recurrent paralysis later.

Radiological Features: The frequent failure to diagnose these tumors is due partly to inadequate roentgen examination and in part to the fact that the possibility of a paravertebral extension is not considered and looked for in the roentgenogram. In his latest analysis of a five-year series of spinal tumors at the Mayo Clinic, Camp found that 30.3 per cent showed bone changes (Am. J. Roentgenol. **40:** 540, 1938). The first result of compression in intradural tumors is a flattening and loss of convexity of the inner surfaces of the vertebral pedicles in the anteroposterior film.

Enlargement of foramina is unusual, but slight degrees of widening are occasionally found. If the tumor is extradural the erosion is chiefly felt in a foramen, which is enlarged in all directions. In the lateral films there is noted an increased vertical interpedicular distance. Once the tumor has escaped from the foramen or between the laminae, a paravertebral opacity is produced and shows as a rounded shadow centering over an enlarged foramen and arising from the spine. As the paravertebral tumor grows, destruction of transverse processes and vertebral spines is produced.

Treatment: In the presence of spinal cord compression, the dumb-bell tumors should be approached first by laminectomy, in order that the paralysis may be relieved. In the absence of paralysis it is possible to remove the whole tumor, using a paravertebral approach and enlarging a foramen. MAX CLIMAN, M.D.

THE GENITO-URINARY TRACT

Prognosis in Bilateral Renal Tuberculosis. W. F. Braasch and E. B. Sutton. J. Urol. **46:** 567–578, October 1941. Also in Canad. M. A. J. **45:** 320–325, October 1941.

Our previous concepts concerning life expectancy in cases of non-surgical bilateral renal tuberculosis demand radical revision. In spite of advanced involvement, the combined renal function often is normal or reduced only slightly. A surprisingly large number in the authors' series of non-surgical patients with bilateral renal tuberculosis survived for ten and even fifteen years. Therefore, if the advisability of operation in a given case is debatable, the possibility of long survival without surgical intervention must be considered.

There is a decided difference among urologists as to the type and degree of evidence deemed necessary to establish a diagnosis of bilateral renal tuberculosis. In some of the cases bilateral retrograde pyelography will be necessary to recognize the lesion. The urographic deformity may be so slight in these cases that it will be missed completely in the excretory urogram.

A considerable degree of ureterectasia often may be noted, especially in the lower thirds. It is easy to understand how tubercle bacilli, washed up from the bladder, can be picked up from the dilated ureter by the ureteral catheter and thus apparently indicate bilateral renal tuberculosis when the disease is actually unilateral. For this reason, the authors state, the presence of Mycobacterium tuberculosis in the renal urine obtained by catheterization, as determined by positive inoculation of guinea-pigs, is not sufficient. There should be also at least 3 to 10 pus cells per high-power field and, in some cases, positive urographic deformity in order to make the diagnosis certain.

Nephrectomy in cases of bilateral renal tuberculosis is indicated only when there is a decided difference in the extent of the lesions in the two kidneys. Even under such circumstances nephrectomy would not be indicated unless the diseased kidney was the cause of symptoms. Thus in the twenty-five years, 1910 to 1934, of the 291 cases of bilateral renal tuberculosis observed in the Mayo Clinic, only 87 submitted to nephrectomy. Study of the remaining 204 proved cases is the subject of this report.

The incidence of unilateral renal tuberculosis among males was twice that among females, while the incidence of bilateral renal involvement among males was twice as great as of unilateral disease. A clear-cut history of a period of dysuria and frequent micturition many years prior to examination, with a recent recurrence of symptoms, is frequently elicited and is typical of bilateral tuberculosis. Cystoscopic examination usually reveals a greater degree of involvement of the bladder than with unilateral disease.

Roentgenographic studies revealed areas of renal calcification in 19.6 per cent of the cases. The calcification was variable in degree, but on the whole was more massive than that seen in unilateral cases.

The occurrence of previous tuberculosis in other tissues often seems to increase the patient's resistance and may be accompanied by a relatively good prognosis.

The incidence of hypertension in cases of bilateral renal tuberculosis is little higher than the average incidence of hypertension observed among adults. It is evident that the changes in the renal tissue secondary to tuberculosis, even when bilateral, do not affect the vascular supply with secretion of pressor substances, as in cases of pyelonephritis.

The subsequent clinical course was traced in 167 cases in which definite clinical evidence of bilateral renal tuberculosis was present. The survival rate of patients traced after three years or more was about 72 per cent; for five years or more, 58 per cent; for ten years or more, 26 per cent; and for fifteen years, 16 per cent. Most of the patients who were living ten or fifteen years after examination were in a fairly normal condition except for a variable degree of frequent urination.

Therapeutic measures, such as treatment in a sanatorium or the advantages of rest, diet, and sunshine, are undoubtedly factors in aiding longevity. Unless the indications for nephrectomy are quite definite in a case of bilateral disease, it would be well to give nature a chance. BENJAMIN H. ORNDOFF, M.D.

Roentgen Demonstration of the Prevesical Spaces. Bernard Strauss. J. Urol. **46:** 520–527, September 1941.

Employing the double contrast principle, injecting diodrast or skiodan between the pubis and the air-filled bladder in living patients, the author studied the various prevesical spaces to which Retzius' name has been indiscriminately applied. Air cystograms demon-

strated the various shapes assumed by the contrast material as it flowed between fascial planes, outlining the retropubic, preperitoneal, and prevesical spaces. However, the space into which the injection was made, or the direction the solution would take, could not be predicted. The procedure was not difficult and no complications were encountered.

The author points out the importance of these spaces in all operations upon the bladder and in infections and inflammations. Normal variations suggest how widespread infections in this area may become, and how they may "point" in distant sites.

The peritoneal fold was shown to be not markedly raised by the distended bladder. It is, however, constantly 2 to 3 cm. above the pubis, permitting the customary extraperitoneal approach to the bladder.

BENJAMIN H. ORNDOFF, M.D.

MISCELLANEOUS

Interstitial Emphysema in Diabetes Mellitus Due to Colon Bacillus Infection: Report of Four Cases. Carl L. Gillies. J. A. M. A. **117:** 2240–2242, Dec. 27, 1941.

The development and spread of gas in the soft tissues is usually considered prima facie evidence of anaerobic gas bacillus infection. It is not generally appreciated that colon bacilli either alone or in association with other aerobic bacteria can, in a patient with diabetes mellitus, produce interstitial gas and the severe constitutional symptoms characterizing gas gangrene. Hitschmann and Lindenthal in 1899 concluded that the colon bacillus produces interstitial gas only in the presence of diabetes.

The author has seen 4 cases of this condition within two years, and believes that the incidence is higher than the dearth of reported cases would indicate. Of the 4 cases, one illustrates gas formation in the kidneys and perirenal areas. Another showed gas in the thighs after operation for carcinoma of the rectum; another gas in the tissues about the ankle, associated with diabetic gangrene of the foot. The fourth patient had an infection of the thigh at the site of an injection of insulin, with gas in the upper part of the thigh. Cultures in each instance showed the presence of colon bacilli. In some cases other organisms were associated with the colon bacillus, but none showed the presence of anaerobic bacteria.

It seems logical to assume that the presence of an increased dextrose content of body fluids and tissues offers a situation favorable for the production of gas by the colon bacillus.

Attempts to produce interstitial gas experimentally by injecting strains of the colon bacillus in the leg of a depancreatized dog were unsuccessful.

The author concludes that the possibility of colon bacillus infection should be considered first with any diabetic patient showing signs of infection and the presence of interstitial gas.

CLARENCE E. WEAVER, M.D.

RADIOTHERAPY

MALIGNANT TUMORS

Malignant Tumors of the Testicle. John K. Ormond and Charles L. Prince. J. Urol. **45:** 685–691, May 1941.

The authors have presented an excellent review of many of the important known facts and controversial issues in regard to testicular tumors and discussed them in relation to their cases. A total of 21 malignant testicular tumors seen in the Henry Ford Hospital since its founding in 1915 were surveyed. The authors conclude that (1) the presence or absence of demonstrable metastases is of great prognostic significance; (2) that adequate x-ray therapy is of great importance.

The age incidence, duration of symptoms, locations and routes of metastases, and differential diagnosis are discussed. Trauma is probably not a factor of importance in etiology. Pathologists disagree on histologic classification, one school calling these tumors all teratomata, the other differentiating two types, teratomata and seminomata.

There are at present five methods of treatment: orchidectomy alone; deep x-ray therapy alone; radical orchidectomy with removal of the draining lymphatics; orchidectomy followed by deep x-ray therapy; orchidectomy with preoperative and postoperative x-ray therapy.

The first three methods are used by only a few. The last two are those most widely advocated, and seem to have about an equal number of adherents. In reporting results of treatment in this series, the cases were divided into two groups. The first, those with no demonstrable metastases when first seen, included 10 patients. Of these, only 2 are known to be dead and 5, or 50 per cent, have already lived more than five years. Eleven patients had evidence of metastases when first seen. Of these, all are dead except one, who is living after five months. Orchidectomy with postoperative deep x-ray therapy was the treatment given most cases in the latter class. The authors feel that an inadequate amount of x-ray treatment was probably given.

BENJAMIN H. ORNDOFF, M.D.

NON-MALIGNANT CONDITIONS

Roentgen Therapy for Bronchiectasis. Ralph C. Carpenter, H. Dabney Kerr, and J. S. McMurray. Arch. Otolaryng. **34:** 913–919, November 1941.

The authors have treated a series of 38 cases of chronic bronchiectasis by roentgen rays. In all the disease had been present for months or years and various therapeutic measures had been tried. Diagnosis was in every instance unequivocally established by bronchoscopic and bronchographic study and cultures of aspirated secretions. The treatment factors were as follows: 200 kv.; 50 cm. distance; 0.5 mm. copper filtration; field size 10 × 10 cm. for children, 10 × 15 cm. for adults. The average total dose for each field varied from 1,200 to 1,700 r. Treatment was given through anterior, lateral, and posterior fields. The average daily dose varied from 100 to 200 r, given through two fields. The treatments usually were completed in three weeks. In the cases in which there was bilateral involvement, only one side was treated at a time; after a period of several months, the other side was treated.

No striking improvement was obtained, although a small percentage of patients received some benefit, at least during the period of observation. The best results were obtained in those with minimal and moderate involvement.

X-Rays in the Treatment of Acne Vulgaris. H. G. Miskjian. Ohio State M. J. **37:** 1177–1179, December 1941.

The author stresses x-ray therapy as the outstanding and most successful method of treatment for acne vulgaris. He disparages the trial of all other methods first, with resort to irradiation only as a last measure. Acne rosacea and acne with small papules (which may be due to Demodex infestation) are relatively resistant to x-rays, but the other common types respond most favorably. Care should be used, however, in ad-

ministering x-ray therapy to persons under eighteen years or those giving a history of previous x-ray therapy.

The author's technic calls for 80–100 kv., 0.5–1 mm. aluminum filter, 10 inches F.S.D. Three fields are used, one on each side of the face and a third over the forehead, with a lead rubber shield for the eyes and eyebrows and to prevent overlapping of the fields. Eight treatments are given two weeks apart, 150 r per treatment.

SIMON POLLACK, M.D.

INJURIOUS EFFECTS

Bladder Injury Subsequent to Irradiation of the Uterus. Archie L. Dean and Danely P. Slaughter. J. Urol. **46:** 917–924, November 1941.

The authors refer to a previously published analysis (Dean) of 3,041 patients treated with irradiation for uterine and ovarian diseases, in which 2.48 per cent later sought relief because of injured bladders. The incidence varied with the disease treated, being least (0.38 per cent) for fibromyoma uteri and greatest (7.31 per cent) for postoperative recurrent carcinoma of the cervix.

Radium applications caused most of the subsequent bladder damage. The effects of roentgen therapy appeared relatively insignificant. As yet no satisfactory way has been found to protect the bladder.

The pathologic changes are interstitial fibrosis in the bladder wall and an obliterative endarteritis occluding nutrient arteries. The blood supply to the bladder wall is thus impaired and trophic ulcers or occasionally fistulae result.

Because these changes are usually of slow development, patients are likely to have no bladder distress for a number of years after the uterus has been treated. For this reason these bladder injuries occurred almost exclusively in patients cured of the primary uterine disease. The onset of symptoms was sudden. The patient suffered acutely with dysuria, frequency, and hematuria. Cystoscopic examinations usually revealed single areas of ulceration surrounded by acute inflammation. Slough covering the surface was frequently impregnated with calcific deposits. Both the mode of onset and the cystoscopic picture suggest carcinoma.

The authors found that drugs of the sulfonamide group, appropriately chosen on the basis of cultures of the bladder urine, gave prompt relief. This was in marked contrast to unsatisfactory results of the former treatment by months of lavage, instillations, and general supportive measures. The crux of treatment was the presence or absence of infection. Despite the persistence of the ulcer, the associated symptoms promptly subsided when infection was eliminated. Women with sterile urine feel quite comfortable even though ulcers of considerable size may still be present.

BENJAMIN H. ORNDOFF, M.D.

EXPERIMENTAL STUDIES

Effect of Hard Roentgen-Rays on Intestines of Normal Dogs Fed on Inorganic Iron Compounds. Y. K. K'o, C. L. Tu, and B. C. Chan. Surg., Gynec. & Obst. **73:** 333–340, September 1941.

The authors undertook to determine experimentally whether or not inorganic iron compounds can be safely administered orally in full therapeutic doses to patients who must undergo prolonged irradiation of the abdomen or pelvis with hard roentgen rays. Such a study they believe has a definite bearing in cases of carcinoma of the cervix associated with anemia of moderate or extreme severity.

The experiments were carried out in female dogs and the irradiation factors, except for field size, were approximately those used in cervical carcinoma cases at the authors' clinic (Peiping Union Medical College): 200 kv., 8 ma., 50 cm. skin target distance, 0.5 mm. copper and 2 mm. aluminum filtration, 1.145 mm. half value layer in copper, 4 abdominal fields 8 × 6 cm. (instead of 16 × 10 cm.). A daily dose of 100 r was given through each of two ports daily, with a total dosage of 2,400 r in twenty-four days. Four animals served as controls, 2 being irradiated but receiving no iron and the other 2 receiving therapeutic doses of ferrous sulphate and ferric ammonium citrate. Four animals were irradiated and received ferrous sulphate (0.75 gm. daily) and 4 were irradiated and received ferric ammonium citrate (6 gm. daily).

The results of the experiments and the conclusions based on these are well summarized by the authors. They are as follows:

1. Normal dogs irradiated through the abdomen by a protracted course of roentgen rays for a total depth dose of 2,400 r showed no clinical symptoms during the course of treatment and no pathological change of the small intestine at the end of the irradiation.

2. The daily administration of ferrous sulphate or ferric ammonium citrate in the therapeutic dose, throughout the period of irradiation, tended to increase the blood hemoglobin.

3. Clinically there was no significant sign of intoxication in dogs irradiated and treated with either the ferrous or ferric compound.

4. Pathological examination of the small intestine showed a mild degree of edema and congestion of the mucosa in those animals irradiated and treated with ferrous sulphate. These changes disappeared completely in a period of eight weeks.

5. In those irradiated and treated with ferric ammonium citrate there was more edema, and large hemorrhagic areas were present in the mucosa of the small intestine. These diffuse, severe hemorrhagic lesions persisted for at least eight weeks after completion of the roentgen irradiation.

6. The data presented serve to indicate that ferrous sulphate is definitely valuable in the treatment of the anemia as a result of chronic blood loss and it is harmless to the small intestine while the animal is undergoing abdominal roentgen irradiation. Ferric ammonium citrate when given in its therapeutic dose is irritative to the intestinal mucosa under similar circumstances and its use is not recommended.

Note on the Effect of Dermal and Enteral Irradiation by Radio-Phosphorus on the Blood Levels of Dogs. L. A. Erf. Am. J. M. Sc. **202:** 650–654, November 1941.

Radio-phosphorus, which emits only beta rays, as a solution of sodium phosphate, was enclosed in rubber capsules. The skin over the splenic area was exposed in one set of dogs, and the capsules were so fed to another set that one capsule was present in the gastrointestinal tract at all times during the experiment.

In the first group, a beta-radiation "burn" which occurred healed without scarring or return growth of hair. Slight changes were produced in the blood

levels, including a decrease in the absolute number of lymphocytes. Similar but significant changes were produced when the radiation was applied enterally.

It is assumed that the capsules did not remain in the center of the lumen of the enteric canal, and that they moved more rapidly in the small than in the large bowel. Since the greatest amount of ionization occurs just before the termination of the beta ray, and since the radiation was sufficient to kill hair follicles of the skin, it can be assumed that the beta rays reached some of the germinal lymphoid follicles of the gastrointestinal submucosa. Since evidence previously reported showed that the majority of the lymphocytes originate in these follicles, the changes in the blood might be attributed to the effects of the radiation on the follicles.

This paper indicates another approach to the study of the origin of lymphocytes, and suggests the possibility of enteral irradiation in man.

BENJAMIN COPLEMAN, M.D.

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